



# UNITED STATES NAVY

## Medical News Letter

Vol. 52

Friday, 20 September 1968

OCT 14 1968

No. 6

U.S. Army



### CONTENTS

#### MEDICAL ARTICLES

Characteristics of Drug Abusers Admitted to a Psychiatric Hospital .....	1
Predictability of Weight Loss .....	7
Hyperparathyroid Crisis .....	11
Clinical Severity of Tetanus in Narcotic Addicts in New York City .....	14

#### MEDICAL ABSTRACTS

TPI and FTA-ABS Tests in Treated Late Syphilis ..	17
Biology of Myocardial Infarction .....	17
Mortality and Hardness of Local Water-Supplies ...	17
Exertional Rhabdomyolysis in Naval Officer Candidates .....	18
Carcinoma of the Breast .....	18

#### DENTAL SECTION

What About a Vaccine for the Prevention of Dental Caries? .....	18
Early Diagnosis of Oral Cancer .....	19
Personnel and Professional Notes .....	19

#### NURSE CORPS SECTION

Report Regarding Color Coding on Individual Dose Narcotic Packages .....	20
Infection Surveillance Nurse at Naval Hospital, Oakland .....	20

#### PREVENTIVE MEDICINE SECTION

Influenza—Hong Kong .....	21
32nd Annual Educational Conference on Environmental Health .....	21
Outbreak of Tuberculosis—Buffalo, New York .....	22
Parathion Poisoning—Texas .....	22
Rabies .....	23
Contributions of Pesticides Outweigh Health Hazards .....	24
Know Your World .....	26

#### EDITOR'S SECTION

Hodgkin's Disease .....	27
Insect Repellents .....	28
BUMED Film Releases .....	29



United States Navy  
MEDICAL NEWS LETTER

Vol. 52

Friday, 20 September 1968

No. 6

Vice Admiral Robert B. Brown MC USN  
Surgeon General  
Rear Admiral G. M. Davis MC USN  
Deputy Surgeon General  
Captain J. J. Downey MC USN, Editor  
William A. Kline, Managing Editor  
Contributing Editors

Aerospace Medicine ..... Captain M. D. Courtney MC USN  
Dental Section ..... Captain H. J. Towle, Jr. DC USN  
Hospital Administration ..... Captain R. M. Tennille, Jr. MSC USN  
Nurse Corps Section ..... CDR A. M. Byrnes NC USN  
Occupational Medicine ..... Captain N. E. Rosenwinkel MC USN  
Preventive Medicine ..... Captain C. H. Miller MC USN  
Radiation Medicine ..... Captain B. K. Hastings MC USN  
Research Section ..... Captain B. F. Gundelfinger MC USN  
Reserve Section ..... Captain C. Cummings MC USNR  
Submarine Medicine ..... Captain B. K. Hastings MC USN

*Policy*

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, sus-

ceptible to use by any officer as a substitute for any item or article, in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

*Change of Address*

Please forward changes of address for the News Letter to Editor: Bureau of Medicine and Surgery, Department of the Navy, Washington, D.C. 20390 (Code 18), giving full name, rank, corps, old and new addresses, and zip code.

**FRONT COVER: GORGAS MEMORIAL LABORATORY.** The Gorgas Memorial Laboratory, in Panama, is the main operating agency of the Gorgas Memorial Institute of Tropical and Preventive Medicine which is a private incorporated research organization with headquarters in Washington, D.C. The Institute was conceived as a living memorial to General William C. Gorgas in recognition of his outstanding accomplishments in the control of diseases. The Laboratory was established in 1929, and research has been carried on there continuously since then in the field of tropical medicine, with special interest in ecology and epidemiology. It has contributed most of the new knowledge developed on tropical diseases in Panama during the past 40 years. Navy medical personnel have had duty at the Laboratory from time to time and have contributed substantially to the scientific information of a basic and applied nature which has been published in over 400 reports. Among the Laboratory's firsts was a complete survey in Panama of poisonous snakes, worm parasites of horses, ticks and biting insects, and the incidence of snake bites. It also produced a description of some 69 new species of Phlebotomous sandflies, made a detailed study of bot-fly in man, and established the first laboratory colony of *Anopheles albimanus*, the main vector of malaria in Central America. The Laboratory made the first recovery of yellow fever virus in Panama and elucidated its cycle in the jungle, and demonstrated that crab-hole mosquitoes (*Deinocerites*) are hosts for St. Louis encephalitis virus. Since its beginning Gorgas Memorial Laboratory has offered its facilities to visiting scientists, who have stayed from a few days to several years. More than 50 investigators, including many prominent leaders in parasitology, entomology and tropical medicine, have been guests of the Laboratory. Junior and senior medical students frequently visit for periods of 2 to 6 months. Cooperative research programs have been carried on with other research organizations in the Western Hemisphere.

The issuance of this publication approved by the Secretary of the Navy on 4 May 1964.

U.S. NAVY MEDICAL NEWS LETTER VOL. 52 NO. 6

## CHARACTERISTICS OF DRUG ABUSERS ADMITTED TO A PSYCHIATRIC HOSPITAL

*Leon J. Hekimian, MD, and Samuel Gershon, MB, BS,  
DPM, JAMA 205(3):125-130, July 15, 1968.*

One hundred and twelve drug abusers admitted to Bellevue Psychiatric Hospital were studied from a social, motivational, psychiatric, and pharmacological view. Heroin users were usually sociopathic and were costing the city \$10 million a day in crimes to support their habit. Emotionally disturbed but younger groups tended to use marihuana, amphetamines, and hallucinogens. Fifty percent of this group were considered to be schizophrenic before taking drugs and 37 percent required state hospitalization. Thus, protracted psychotic states thought to be due to drug ingestion may be due to preexisting mental disturbances. A desire for euphoria, possibly stemming from underlying depression, was most frequently the reason given for drug abuse. Influences by friends or environment was the second most frequent reason. Almost all patients had experiences with drugs other than the one which caused admission to the hospital.

The problem of drug abuse has become important in large municipal facilities like Bellevue Psychiatric Hospital where admissions for drug abuse, always a significant number, have been increasing recently. This survey of 112 hospitalized drug abusers was undertaken from the following points of view: (1) general characteristics of drug abusers; (2) motivational factors and drug use patterns resulting in the current hospitalization; (3) effect of the current drug episode on the predrug psychiatric status; (4) documentation of the psychiatric diagnosis and disposition.

### Materials and Method

One hundred and twelve Bellevue psychiatric patients with an admission history of drug abuse were evaluated in this study (January through July 1967). This number was a random selection (one in five hospitalized drug abusers, or 5 percent of total

admissions). Patients were included if one of the following drugs was taken within 48 hours prior to admission: (1) narcotics (heroin, morphine); (2) marihuana; (3) amphetamines (methamphetamine [Desoxyn, Methedrine], dextroamphetamine [Dexedrine] sulfate); (4) hallucinogens (lysergic acid diethylamide [LSD], 2, 5-dimethoxy-4-methylamphetamine [STP], and dimethyltryptamine [DMT]; (5) miscellaneous drugs (barbiturates, cocaine, glutethimide [Doriden]. The history from the patient, referring agency, or accompanying person was accepted as documentation for the drug abuse. The patients were grouped according to the drug responsible for the admission. All patients admitted were psychotic, in a toxic condition, or came for drug withdrawal. One of three was admitted voluntarily or referred by family friends, police, or a social agency.

Each patient was interviewed jointly within 24 hours of admission by two senior psychiatrists. The interviews were structured to provide information for a standard case report form devised for this study. The form provided (1) demographic and social data; (2) drug dependence history; (3) psychiatric history, (4) motivational factors, psychiatric illness before taking the drug, and the drug effects at admission; (5) present hospital course, final psychiatric diagnosis, and disposition. Patients whose history was not clear at the initial interview were interviewed a second or third time. Observation was one to two weeks in length. All medications were discontinued unless patients were acutely disturbed.

That there were limitations to such a study was initially apparent. Histories were not always reliable, and psychiatric diagnoses were complicated by symptoms produced by the drug. Absence of laboratory methods to confirm drug ingestion was also a deficit. However, it was felt that a survey of the characteristics of drug abusers here might suggest leads for subsequent more intensive studies.

From the Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University School of Medicine, New York. Reprint requests to 550 First Ave, New York 10016 (Dr. L. Hekimian).



Table 1.—History and Preadmission Data

Patient Group, No.	Mean Age, Yr	Patient's Reason for Taking Drugs:													Predrug Psychiatric Diagnosis			
		Sex			Family History of Drug Abuse or Psychiatric Treatment	Desire for Euphoria	Influenced by Friends or Environment	Curiosity	Other Reasons or None	Other Drugs Taken by	Previous Psychiatric Treatment	Schizophrenia	Sociopathic Personality	Other Personality Disorder	Depression, Neurosis, or Other			
		M	Sex	F														
Heroin																		
22	29.5	21		1	*	*	*	*	*	19	*	2	11	2	7			
10	29.9	10		0	2	6	2	2	0	9	7	0	3	2	5			
Marihuana																		
8	24.4	6		2	1	3	4	0	1	6	7	6	0	1	1			
Amphetamine																		
22	24.8	18		4	5	12	4	2	4	18	13	9	4	2	7			
Hallucinogen																		
47	22	34		13	12	19	9	12	7	40	24	23	6	10	8			
Miscellaneous																		
13	31.3	5		8	0	8	3	1	1	12	11	3	3	2	5			

\*Complete data was not obtained.

Table 2.—Admission and Postdrug Ingestion Data

Patient Group, No.	Patients' Subjective Effects or Responses		Effect of Drug Ingestion on Admission			Final Psychiatric Diagnosis					Disposition	
	Favorable	Unfavorable	Psychosis or Increase of Psychopathology	Symptoms Relieved or No Effect	Criminality Associated With Drug Abuse	Schizophrenia	Sociopathic Personality	Other Personality Disorder	Depression, Neurosis, or Other		Hospitalization	Home
Heroin												
22	*	*	*	*	*	3	15	1	3		4	18
10	10	0	9	1	7	1	6	1	2		2	8
Marihuana												
8	5	3	7	1	0	6	0	1	1		4	4
Amphetamine												
22	16	6	22	0	4	11	5	2	4		8	14
Hallucinogen												
47	15	32	43	4	6	32	6	4	5		16	31
Miscellaneous												
13	10	3	13	0	4	3	5	0	5		2	11

\*Complete data was not obtained.

## Results

**Heroin Group.**—Table 1 shows predrug data and demographic characteristics of 22 heroin patients (15 white and seven Negro), with mean age of 29.5 years, and a mean duration of addiction of 8.6 years. The most frequent preheroin psychiatric diagnosis was sociopathic personality disorder, of which there were 11. Additional findings were that 19 had tried other drugs before or with their heroin and 12 of these had taken marihuana.

Table 2 shows the postdrug ingestion data. The final psychiatric diagnosis, in addition to the heroin addiction, was made prior to disposition from hospital for the 22 subjects. These diagnoses now included 15 sociopathic personality disorders, as four heroin addicts had resorted to criminal acts to support the habit. Final disposition included 18 discharged home, usually within one week, and four for state hospital commitment.

Of the 22 admitted who used heroin, the first ten were studied intensively to determine additional elements in their profiles. The mean level of edu-

cation was 9.2 years. Two of the ten reported psychiatric illness in parents or siblings and eight were living alone at the time of admission. The reasons for taking heroin included "to get high," "relief of depression," "feel normal," etc. (In this study such responses were grouped as "desire for euphoria.") Six of the ten gave replies in this category and four gave the following as their reasons for taking the drug: "curiosity," "influenced by friends," or "influenced by environment." These responses were typical of those from other heroin addicts admitted to Bellevue Psychiatric Hospital, who are not included in this study.

The amount of heroin intake on admission ranged from 3 to 40 packs a day at \$5 per pack. For the ten patients, the mean daily cost was \$75. Seven of the ten patients acknowledged resorting to criminal behavior, including larceny, forgery, prostitution, or pushing drugs.

**Marihuana Group.**—There were eight patients who took marihuana (six males and two females; six white, one Negro, and one American Indian).



The mean level of education was 11.5 years (two years higher than for the heroin group); seven were living alone and all eight were either employed or students. The mean number of years of marihuana use was five.

The reasons for smoking marihuana included influence by friends or environment (four), a desire for euphoria (three), and no reason (one). Six had experimented with LSD. One female had reputedly taken LSD 2,000 times with an average dose of 300 $\mu$ g. She had often combined LSD with amphetamine and had smoked marihuana for ten years. She was admitted while under the influence of marihuana.

Seven of eight patients had had previous psychiatric hospitalization or treatment. Six of the eight patients described primary and secondary symptoms of schizophrenia prior to smoking marihuana. One was a schizoid personality and one was a depressive prior to smoking marihuana.

Subjective effects reported by the patients (Table 2) included favorable effects in five (felt "pleasant" or "calm") after smoking marihuana. These patients also acknowledged becoming psychotic (having delusions or hallucinations) or a worsening of their preexisting psychotic symptoms. Four displayed undifferentiated reactions and one was paranoid on admission.

The final diagnosis of the eight patients who took marihuana indicated six with schizophrenic reactions, one schizoid personality disorder, and one acute brain syndrome due to marihuana. Four of the eight improved sufficiently for discharge but four were detained for state hospital commitment.

*Amphetamine Group.*—Demographic data (Table 1) on this group of 22 showed 18 males and four females, 21 of whom were white, and one Negro. The mean age was 24.8 years; mean attained education, 11 years; 17 were employed, students, or housewives; and 14 of the 22 were living alone.

The mean duration of amphetamine intake for the group was 3.4 years. Fourteen of the 22 were taking amphetamine in the form of dextroamphetamine; combinations of methamphetamine (Desoxyn, Methedrine) and a mixture of dextroamphetamine sulfate and amobarbital (Dexamyl) were also used. Specific dosage could be determined in only 13. The mean daily dose for this group was 780 mg/day (range, 30 mg to 5,000 mg, taken orally and intravenously). The latter patient was a 24-year-old white man who had started taking marihuana at 17 years of age, switched to LSD at 21, and then combined LSD with

amphetamines taken orally and intravenously "to complement the acid effects." During his use of amphetamines, he acknowledged taking 200 to 300 LSD "trips" in three years with doses of 300 $\mu$ g to 500 $\mu$ g. During hospitalization, drowsiness, mild paranoid trends, and some bizarreness were seen, all characteristics of withdrawal from amphetamines.

Eighteen of the 22 amphetamine users had used other drugs (marihuana or hallucinogens) and 13 had had previous psychiatric treatment or hospitalization (Table 1). Preaddiction diagnoses included nine users who described signs of schizophrenia, six who showed neurotic patterns, and four who were known sociopathic personalities prior to taking amphetamine.

The most frequent reason for taking amphetamines was a desire for euphoria (Table 1). Twelve patients gave such responses as "to get high" or "because of depression." Six said influences of friends, environment, or curiosity were the reason, while three stated "for more self-awareness." One patient used the drug for dieting.

Favorable subjective effects were reported by nine (Table 2), while seven stated that they related better or were aware of themselves or were stimulated. Five acknowledged becoming psychotic with not too much concern. One patient stated there was "no effect." However, all 22 amphetamine users were considered by us to be worse as a result of their drug ingestion. On admission 16 showed either an increase in their preexisting psychotic symptoms or had a paranoid psychosis from amphetamine intake. Six showed an increase in their preexisting antisocial behavior or became overtly sociopathic. The sociopathic behavior was less severe than with heroin users. Four tended toward criminal behavior but this was not conspicuous. Procurement, cost, or withdrawal did not pose difficulties as with the heroin users. The most frequent final diagnoses assigned, in addition to amphetamine addiction, included 11 schizophrenic reactions and five sociopathic personalities. Fourteen patients were discharged and eight were recommended for state hospitalization.

*Psychedelic or Hallucinogen Group.*—Demographic characteristics for the group of 47 psychedelic patients included a mean age of 22 years with 34 males and 13 females (Table 1); 34 were white, and 13 Negro. Twenty-five were living alone and 31 of the 47 were employed, students, or housewives. Twelve had a family history of drug abuse or psychiatric disorder in parents or siblings. The mean educational achievement was 11 years.

Forty-one were admitted with a history of having taken LSD. About half of these had taken the drug only once or twice. Four were admitted after taking STP and two after taking DMT. The average number of trips for the group was 32. The ingested doses of LSD were known by 17 and the mean maximum single dose was 690  $\mu$ g. One schizoid patient claimed that he had taken 400 LSD trips in two years, with 1,500  $\mu$ g the usual dose.

The following were the reasons given for taking the hallucinogen: a desire for euphoria (19 ["get high" or "relieve depression"]), curiosity (12), influenced by friends or environment (nine), "for self-awareness" (three), and no reason (four). All but seven patients acknowledged taking other drugs previously. Twenty-eight of these had taken marihuana. A significant finding in the psychedelic group was that 24 had had previous psychiatric treatment or hospitalization. Preexisting psychiatric diagnoses prior to drug ingestion included 23 who gave evidence of schizophrenia and ten with schizoid or other personality disorders.

The effect of the drug-abuse episode on the preexisting psychiatric status was seen in 43 of the 47 who were diagnosed by us as psychotic on admission (Table 2). Fifteen patients considered themselves to have had a favorable reaction ("good trip"), but four still sought admission even though they were not psychotic. Only six of 47 had displayed any criminal or sociopathic behavior. Thirty-one patients had exaggerations of their preexisting psychotic phenomena or displayed a schizophrenic reaction which resulted in their hospitalization. Paranoid reactions predominated.

During their hospitalization, 27 of the group had a complete or nearly complete remission of their symptoms whether due to drug ingestion or to the preexisting psychiatric illness. However, 16 ultimately were recommended for state hospitalization while 31 were discharged home. Final diagnoses given the psychedelic group included schizophrenia (32), sociopathic personality (six), and schizoid personality (four). The remaining five patients were diagnosed as depressives or psychoneurotics.

*Miscellaneous Group.*—A miscellaneous group of 13 drug abusers (mean age 31.3 years) included six who took barbiturates; three who took cocaine, two who took glutethimide, and one each who took a trichlorethylene cleaning fluid (Carbona) and dextromethorphan (Romilar) hbr. A mixture of amobarbital and secobarbital (Tuinal) was the barbiturate of choice for six patients. The patient who

inhaled the cleaning fluid was a boy 15 years with two similar previous admissions.

Reasons for the drug ingestion were desire for euphoria (eight), influences by friends or environment (three), curiosity and insomnia (one each). All six barbiturate users reported favorable subjective effects as did the two patients who took glutethimide and the one who inhaled cleaning fluid (Table 2). Nearly all had experimented with other drugs, usually heroin or marihuana. Eleven had been admitted to a psychiatric hospital previously for drug abuse. The preaddictive psychiatric diagnoses included schizophrenia (three) and sociopathic personality (three).

The drug ingestion episode had resulted in sociopathic behavior or psychotic reactions for ten, while acute brain syndromes developed in three (Table 2). Four of the barbiturate users resorted to criminal acts in their drug pursuits. Only two of the 13 needed state hospitalization. This group might reflect the large group of drug users in the functioning and employed middle classes.

#### Comment

The data from the heroin group presented issues that have been associated with hard-core narcotic addicts. Their mean age of 29.5 years was older than that of other drug abuse groups, with males predominating 21 to one. One speculation for the sex difference is that females would depend on male partners for their supply. Furthermore, the needs of females might be limited such that prostitution provided adequate income for the cost of the heroin. In all probability, prostitution was less open to detection than male criminal methods of support.

The preheroin-addiction sociopathic personality disorder evidenced in 11 of our 22 patients was consistent with reported statistics. With addiction, however, an additional four became sociopathic in behavior so that a final diagnosis of sociopathic personality was given to 15 of 22.

The postaddiction criminality rate was seven out of ten with a mean daily expense of \$75 to support the habit. The economic implications of urban heroin addiction became staggering when one considers that New York City has been estimated to have 100,000 narcotic users. The cost of procuring heroin in New York City might be \$10 million per day (obtained mainly by illegal means).

There was no evidence that narcotic addiction had a genetic or familial basis. Vaillant reported that 24 percent of his series of New York City heroin



addicts had an addicted relative. Our group showed a 20 percent incidence of a family member (parent or sibling) with a narcotic history. It seemed that an endemic, environmental, or contagious factor superimposed on a sociopathic character defect appeared to be the combination associated with heroin intake.

Our findings supported the hypothesis of Eddy et al that narcotic addiction has a strong psychic dependence factor based on the desire for euphoria or avoidance of psychic pain. Although depression as an overt reason for addiction to narcotics was not given, when questioned as to the subjective effects (Table 2) narcotic addicts gave replies such as "felt normal," "felt good," or "forgot problems." However, nine of the ten also either became psychotic or criminally sociopathic in their pursuits. Such responses suggested that a depressive component is temporarily relieved by the drug. The characterological aspect of the depression is a factor in the subsequent dependence, tolerance, and the need for replenishing supplies at all costs as is the fear of withdrawal symptoms. Fifteen of our patients were hospitalized voluntarily for withdrawal from heroin.

The striking features in the patients who took marihuana were a high predrug incidence of schizophrenia and relatively great need for further hospitalization. In spite of the severity of the emotional disturbance, five of the eight patients were employed and two were students. Like the heroin group, the majority were living alone. Conspicuous was the lack of any criminal records. The problems of cost and procurement of the drug were not factors with which these patients had to contend.

The findings in the marihuana users supported the suggestion of other investigators, that the use of marihuana is disproportionately higher among unstable persons or those with an established psychiatric entity than among those without these characteristics. Our patients did not display a characteristic marihuana psychosis. The schizophrenics were paranoid or undifferentiated on admission, but several days later, when there no longer were drug effects, their illnesses were well documented.

Among the amphetamine users, as with the heroin and marihuana groups, the low percentage of females was conspicuous. Their dependence on male partners and their prostitution, previously mentioned, might be other factors in the low frequency, and more women resort to alcohol addictive states than is perhaps realized.

Second, schizophrenia was prevalent; 50 percent of the amphetamine and marihuana users were schizophrenics before taking these drugs. Patients with a psychotic process in the predrug period seem to prefer these hallucinogenic drugs which are also more available to them. Heroin users were more often sociopathic in the preaddictive phase and their subsequent linkage to narcotics was more likely. Perhaps the sociopath feels his need for antisocial behavior, so he is prone to seek an addiction that is illegally trafficked and requires criminal behavior for its support.

Third, state hospitalization rates were higher for the amphetamine group (eight of 22). This might be expected since the preaddiction incidence of schizophrenia was higher in the first two groups and the preaddiction incidence of sociopaths was higher in the heroin group. These findings further suggest that a psychotic process is more often associated with the use of marihuana and amphetamine than with heroin, or that the two former drugs have more psychogenic properties than heroin, after years of ingestion.

That amphetamine psychoses produce a conflicting clinical picture was also apparent. Acute reactions resembled paranoid schizophrenia but there were differentiating features. The psychotics who took amphetamines tended to be more fluid and shifting in their delusions and affect. Hyperactivity and hypersensitivity to stimuli frequently with a phobic quality, were other features. Of 22 patients admitted as amphetamine addicts, nine were thought to be schizophrenic before they became amphetamine users. With a significant number of amphetamine users who were also psychotics, one may be dealing not only with amphetamine-affected brains, but also with amphetamine-affected brains which were schizophrenic before the drug was ingested. This combination of factors might explain the confusing clinical picture that the psychotic amphetamine addict sometimes presents.

A differentiating characteristics of the psychedelic group was the higher percentage of females (28 percent). A striking feature, as with the marihuana and amphetamine groups, was the high percentage of preexisting schizophrenia. Some investigators and the press have referred to the prolonged adverse reactions to LSD. However, there was increasing evidence that the prolonged or recurrent psychotic episodes were not simply due to pharmacological effects of the LSD ingestion. Our findings generally supported those of Blumenfield and Glickman. For

Table 3.—Prominent Features of Each Drug Group

Patient Group, No.	Patients' Reason for Taking Drug (%)	Other Drugs Taken by (%)	Previous Psychiatric Treatment (%)	Predrug Psychiatric Diagnosis (%)	Patient's Subjective Response to Drug (%)	Psychosis or Increased Psychopathology Due to Drug (%)	Criminality Associated With Drug (%)	Final Psychiatric Diagnosis (%)	Disposition (%)
Heroin 22	Desire for euphoria 60	87	70	Sociopathic personality 50	Favorable 100	90	70	Sociopathic personality 68	Home 82
Marihuana 8	Friends or environment 50	75	88	Schizophrenic reaction 75	Favorable 63	88	0	Schizophrenic reaction 75	Home 50
Amphetamine 22	Desire for euphoria 55	82	59	Schizophrenic reaction 41	Favorable 73	100	18	Schizophrenic reaction 50	Home 64
Hallucinogen 47	Desire for euphoria 40	85	51	Schizophrenic reaction 49	Unfavorable 68	66	13	Schizophrenic reaction 68	Home 66
Miscellaneous 13	Desire for euphoria 62	93	85	Depression or other 38	Favorable 77	100	31	Sociopathic personality 31 Depression or other 31	Home 85

instance, the fact that almost 50 percent of the hallucinogen group showed signs of schizophrenia or were treated for that condition before taking LSD must be considered a significant factor. Another ten of the group showed schizoid features prior to the hallucinogen intake. In addition, there was a high incidence (40 of 47) of other drug abuses (marihuana, amphetamine, and heroin) prior to hospitalization for LSD effects. Thus, the issue becomes obscured. Are prolonged adverse psychotic reactions to the psychedelic drugs due to the drug per se, or are they in fact often due to the preexisting psychiatric illnesses, plus other drug insults, plus the final insult of several LSD trips?

The high crossover incidence of marihuana use to use of hallucinogens was conspicuous. Twenty-eight of our 47 patients were once marihuana users. Also, six of our eight marihuana users had previously taken LSD. Drug abuse, except for the sociopathic heroin group, is experimental, crossover, and polymorphous and in our study, there was high incidence of serious preexisting psychiatric disturbance.

Those who used psychedelic drugs also searched for euphoria; 19 of the 47 gave this response. The search for euphoria again suggests that large numbers of all drug abusers have inherent depressive factors in their personality. Perhaps the relationship of depression to drug abuse should be more systematically and critically explored.

### Conclusions

The increasing urban problem of drug abuse is reflected by this study of 112 drug abusers admitted to a psychiatric hospital between January and

July 1967. One of every five narcotic, marihuana, amphetamine, or psychedelic drug abusers admitted was evaluated with a standardized case report form to determine characteristic social, motivational, psychiatric, and pharmacologic factors. Of the 20,000 patients annually admitted to Bellevue Psychiatric Hospital, drug offenders (excluding alcohol and prescribed drugs) represented at least 5 percent of the total admissions. Males predominated by a ratio of four to one.

Heroin users were older as a group and 50 percent were sociopathic personalities prior to their addiction (Table 3). The cost of their addiction in dollars and in crimes becomes a staggering economic and sociological issue.

In addition to narcotic offenders, an increasing number of other drug abusers are becoming hospitalized. A significant incidence of serious preexisting psychiatric disturbance was noted in all groups. Over 50 percent of the patients in the marihuana, amphetamine, and psychedelic groups were considered to be schizophrenic or were treated for the condition before they resorted to their drug ingestion (Table 3). Evidence of the severity of their psychiatric state was the necessity for state hospitalization in 37 percent after their admission for drug abuse. These findings suggest that the protracted psychotic episodes after drug ingestion may be due to the superimposed insult by the drug on a preexisting psychiatric disturbance rather than to prolonged drug effect per se.

Motivations of drug abusers seemed to stem from a desire for euphoria. On admission two out of three patients were living alone. A deep-seated ele-



ment of depression appeared to be a factor common among drug abusers irrespective of the drug chosen. Half of our patients gave "search for euphoria" as their reason for taking drugs. Another reason given was "influence by friends and environment" (22 percent), which suggests a contagious and endemic factor. Almost all patients had experiences with drugs other than the one that caused hospitalization.

One hundred percent of the heroin users had a favorable subjective response to their drug, while the marihuana and amphetamine users were less favorably affected (63 percent and 73 percent, respectively). Only 32 percent of the hallucinogen users stated that they had a favorable subjective response. Psychotic reactions or an increase in psychopathology was highest in the amphetamine users (100 percent) and lowest in the hallucinogen group (66 percent) (Table 3). These were predominately paranoid psychotic or schizophrenic reactions.

In view of the complex of factors, social, environmental, motivational, and psychologic that comprise drug abuse, future studies need to explore these predrug factors as well as the existence of any

psychiatric illness. A comprehensive investigation of clinical depression as it relates to drug abusers would seem important. Under controlled conditions, observations of a drug's effect, metabolism, and excretion and its relationship to concomitant disturbed behavior and thought processes in the addict are major issues. Leads to these ends may require more intensive animal studies directed to understanding habituation and addiction mechanisms and related physiological and biochemical changes. Future clinical studies of drug abusers are essential. These must include chemical identification of the reported drug taken and monitoring of the time course of its excretion in relation to the clinical course of the produced psychosis.

This investigation was supported by Public Health Service Research grant MH-04669.

#### Generic and Trade Names of Drugs

Methamphetamine—*Desoxyn*, *Methedrine*.

Dextroamphetamine—*Dexedrine*.

Glutethimide—*Doriden*.

(The references may be seen in the original article.)

## PREDICTABILITY OF WEIGHT LOSS

*Walter M. Bortz, MD, JAMA 204(2):101-105, April 8, 1968.*

Weight loss is a process that is susceptible to logical and reasonably precise explanation. Consideration of caloric need and caloric supply indicates the weight balance. Any caloric deficit implies weight loss which will occur at the rate decreed by the caloric value (3,500 calories) of a pound of body fat. Whenever this caloric deficit is reached, the body will be one pound lighter, with respect to body fat. When these concepts are used, weight loss becomes predictable. Such predictability offers multiple advantages to the clinician who is preparing a weight reduction program for his obese patient.

The obese patient constitutes one of the most common yet frequently frustrating and disconcerting problems that confronts the practicing physician. The desire of the overweight patient to reduce is not often more than a protestation of little conviction.

The realization of this often shrouds the beginning of a dietary program in the physician's cynicism. This cynicism, no matter how justified, is frequently compounded by the physician's personal lack of knowledge of the factors involved in weight reduction. Present information about weight reduction is often anecdotal or otherwise imprecise. The deluge of proposed dietary regimens and the pseudoscientific rationale with which each is invested only serve to confuse and deny the approach to a scientific basis for weight reduction.

Recent experience with a number of obese patients in the Division of Research metabolic ward of the Lankenau Hospital has indicated that weight change is a process mediated and determined in a precise and predictable fashion. The deviations and fluctuations noted during weight reduction can often be anticipated and logically explained.

The concept of prediction of the rate of weight loss was first proposed by Wilder in 1933. The ideas

From the Department of Medicine and the Division of Research, Lankenau Hospital, Philadelphia.

Reprint requests to the Division of Research, Lankenau Hospital, Lancaster and City Line Avenues, Philadelphia 19151 (Dr. Bortz).

advanced by him and later by Jolliffe and Alpert furnished the basis for this concept. This communication seeks to confirm and extend their precepts.

The body is a fuel-consuming machine which obeys all the classical laws of thermodynamics and requires a specific number of calories for its steady state maintenance. Weight gain occurs when excess fuel, i.e., calories, is consumed; weight loss occurs when there is a deficit of calories. These are the two essentials for the physician to keep in mind when preparing a program of weight reduction: caloric need and caloric supply.

## Methods

Caloric need can be determined in a number of ways. First, a trained dietician can estimate quite accurately the calorie consumption. (Patient reliability and a modicum of intelligence and insight are assumed.) Second, the basal metabolic rate (BMR) can be used to provide an idea of caloric need. The BMR test provides the oxygen consumption value per minute which is then translated to oxygen consumption per day and finally to caloric need per day. Ordinarily, 5 calories are roughly equivalent to 1 liter of oxygen. Some extra calories are added as an allowance for suprabasal physical activities. Third, the monogram of Boothby and Berkson, cited by Jolliffe and Alpert which takes into consideration the factors of sex, age, height, and weight, predicts with adequate accuracy the caloric requirement. In these studies, which were performed in the metabolic ward, all three of these methods were to establish the stabilization requirement, i.e., demand. Results of the three modes of determination usually agree within 10 percent.

The final method of estimation of daily caloric requirement involves simple observance of body weight during extended time periods while the patient is consuming a formula-type diet having an accurately prescribed caloric content.

The second determinant used in calculating the rate of weight loss is the caloric level of the diet, i.e., supply. In our research setting this has been either 600 or 800 calories daily, usually fed in three portions. The timing and the relative composition of the diet in terms of protein, fat, and carbohydrates content are of little long-range consequence.

Knowing the daily caloric requirement necessary for weight maintenance and the number of calories contained in the diet for weight reduction, one can accurately determine the daily caloric deficit (demand minus supply). How is this deficit to be met,

and what are its consequences in terms of weight loss? The human body at any one time contains 200 to 300 gm of utilizable carbohydrate as glycogen and sugar. In time of debit this amount can obviously supply only a minute fraction of a continuing need. Logically then, one might expect protein to serve as a reserve fuel, since it is present in more adequate supply. Protein supplies 4 calories/gm, or roughly 1,800 calories/lb. However, this 1,800 calories is supplied by a pure, unhydrated mixture of amino acids, unknown as such in nature and available only from a powder in a bottle on the chemist's or nutritionist's shelf. Body protein, 80 percent water by weight, would yield only about 450 calories/lb. This clearly is an uneconomic energy supply. Apparently the body is too wise to use this matrix as an energy source. Balance studies indicate that the body in a state of starvation undergoes an initial protein wastage, but then effectively manages to conserve protein, and the amount of nitrogen in the urine falls to low levels. This process has often been observed in undernourished populations.

It can be assumed, then, that fat is the overwhelmingly predominant energy source during periods of caloric restriction. Respiratory quotient measurements repeatedly confirm this fact. Fat is admirably suited to being an energy source, since it has an extremely high caloric content per unit weight. Nine calories per gram equates to 4,000 calories/lb, unhydrated. Fat is only slightly hydrated (15 percent water by weight). The caloric value, therefore, of body fat is 3,500 calories/lb. This is the figure on which all weight gain and weight loss depends. It is the figure that dieters of all types must recognize and understand, for with this figure and the daily caloric deficit, one can predict the rate of weight loss.

An idealized example is as follows: The subject is a 30-year-old housewife who is 162.6 cm (5 ft 4 inches) tall and weighs 102 kg (225 lb). Her daily caloric requirement is estimated to be 2,600 calories to maintain present body weight. Electing a common-sense caloric level of 1,200 for the weight reduction diet, there is a daily caloric deficit of 1,400 calories. This deficit is to be supplied largely by the body fat at the rate of 3,500 calories/lb. Weight loss will therefore occur at the rate of 1,400/3,500 lb day or 0.4 lb/day. If the mirror weight (ideal weight) of this individual is 56.7 kg (125 lb), she has a loss of 45.4 kg (100 lb) planned. At the rate of 0.4 lb/day it should take 250 days to reach



this goal and it will, or will closely enough for any practical purpose. Two hundred and fifty days may seem to be a long period, but it is realistic. It can be shortened only in two ways: (1) increasing caloric demand, and (2) decreasing caloric supply. I have found that increasing caloric demand with exercise is of limited practical advantage in most instances of dieting. Other investigators are more enthusiastic about this aspect, however. A decrease in caloric supply is accomplished by reduction in the number of calories which are consumed daily. The maximal reduction is, of course, total starvation, which would then yield a daily caloric deficit of 2,600/3,500 lb, or roughly 0.714 lb of body weight. At this rate, the 100-lb weight loss will take 140 days. This is the irreducible minimum time required to lose this weight without a marked change in the exercise pattern. One hundred and forty days of starvation is a long, long time. A practicable number of calories, 1,200, is the lowest that seems reasonable, inasmuch as this number is compatible with our social pressures.

There is an additional feature to be considered. Experience indicates that to maintain weight, for each 11.3 kg (25 lb) of excess weight, the body requires 100 calories more than the number required at ideal weight. Conversely, for each 25 lb lost, the caloric deficit will be 100 calories or 0.03 lb less. Therefore, if a great amount of weight is lost, the rate of loss on the same caloric intake will be 0.03 lb/day less for each 25 lb that are lost. For most dieting patients, this consideration may be omitted.

## Results

That this exercise in weight-loss mathematics is more than theoretical can be seen in Fig 1 to 6, (omitted) which represents experience with some obese subjects.

All the information necessary for the prediction of weight loss, (1) the number of calories necessary for weight stabilization and (2) the caloric content of the diet, is presented in Fig 1 to 4 (omitted). The difference between the two is the daily caloric deficit which, when divided by 3,500, yields the daily weight loss in pounds. The dotted lines show this calculation as plotted in anticipation of the low-calorie program. The solid lines show the actual daily weights. These charts are typical of all patients of whom observations were made. In approximately 40 obese subjects observed under strict metabolic ward conditions, the prediction so far has not varied

more than 10 percent from the actual weight loss in any of the subjects.

One cannot expect and should not demand the degree of agreement shown in Fig 1 to 4 (omitted) when dealing with an outpatient. That this capacity to predict weight loss is not confined, however, to the artificial environment of a metabolic ward is seen in Fig 5 (omitted). The patient was a 19-year-old girl whose predicted and actual weight losses were charted. She was an outpatient.

Figures 1 to 5 (omitted) are notable for the accuracy of the prediction. Such accuracy must of necessity involve long-term observation under reliable conditions. Shorter-term observations are often misleading. Figures 3 and 4 (omitted) represent studies in which isocaloric substitution of carbohydrate for fat, in the presence of salt, led to temporary weight plateaus. Apparent deviation from the prediction, therefore, need not implicate cheating on the part of the dieter.

In another obese individual there was a period of 21 days in which no weight was lost whatsoever, despite an anticipated weight loss of 1.2 lb/day, calculated from a 4,200 calorie daily deficit. This period tested the patient's determination and the doctor's faith. The weight-loss prediction was of considerable assistance in reassuring both patient and physician that nothing was amiss. The explanation for this protracted weight plateau in such an extremely obese individual was, of course, fluid retention. This was confirmed by observations of fluid and sodium balance.

A further example of the value of a weight prediction chart follows: Another physician was puzzled by the erratic response of a woman patient's body weight to the vigorous measures he prescribed. Initial testing of thyroid function revealed a somewhat low protein-bound iodine level of 3.6 $\mu$ g/100 ml and a red blood cell triiodothyronine ( $T_3$ ) uptake value of 24.8 percent (normal, 28 percent–35 percent). The basal metabolic rate was +2 percent; however, her serum cholesterol level was only 184 mg/100 ml. After testing, 200 mg of thyroid to be taken daily was prescribed; the dosage was gradually increased to 650 mg daily after the second week. The patient was given dextroamphetamine sulfate capsules (Spansule), in a dose of 10 mg twice a day, which was later increased to 15 mg in the morning and 10 mg at night. Five hundred milligrams of chlorothiazide was given daily. Mercurial diuretics were administered as shown by the arrows at the top of Fig 6 (omitted). Initially, a diet which

contained virtually no calories was prescribed and was liberalized to 600 calories on the 12th day. Weight loss proceeded as seen on the graph. The patient was extremely gratified by her early response. In the first nine days, she lost nearly 17 lb. In the succeeding nine-day periods, she lost 7, 4, 8, and 0 lb. On the 29th day of her program, her physician requested consultation with me because the patient felt that the medicines were no longer working, and her physician felt that she was cheating. A weight-loss prediction chart was drawn retrospectively. Her initial basal oxygen requirement, 251 ml/min (361.4 liters of oxygen per day or 1,807 calories/day), plus a 40 percent activity allowance were used to determine the chart. This yielded a daily caloric deficit of 2,530 calories, since there was no caloric intake. During the first nine-day period, therefore, she should have lost 6.5 lb (2,530/3,500 x 9). Instead she had lost 16.75 lb. On the 12th day, another BMR test showed that the basal oxygen consumption had risen to 309 ml/min or 2,225 calories/day. When a 40 percent activity addition is allowed, the total of 3,115 is derived as the daily caloric need. The new daily deficit can be calculated by subtracting the 600 calories contained in the diet. The observed weight loss is seen to be beneath the predicted lines for the early portion of the program only to approach and nearly meet it later on. This was believed to be due to water loss which led to a false notion concerning the amount of weight lost. Later on, the contracted state of the body fluids had become resistant to persistent diuretic attempts, and weight stabilization occurred.

#### Comment

The early days of any hypocaloric program are characterized by a considerable diuresis in the patient, even in the absence of added diuretics. The actual weight loss then exceeds that predicted. Often a secondary weight plateau is reached, despite continued dieting. This is the result of the body's reconstitution of the early large fluid loss. It must be emphasized, however, that loss of weight due to fat utilization, which is really the essence of the problem, goes on regardless of fluid shifts. Unfortunately, the bathroom scale cannot discriminate between weight due to fat and weight due to fluid. The weight prediction charts are of especial benefit to those individuals who demonstrate an exaggerated fluid-retaining capacity.

Other studies from our metabolic ward have shown that the timing of consumption of the day's calories is not central to the rate of weight loss. Furthermore, any advantage of the low-carbohydrate reducing diets is confined to their dehydrating potential. A number of recent studies have demonstrated the ability of dietary carbohydrate to retain sodium and fluid. Conversely, lack of carbohydrate leads to marked fluid loss. The disadvantage, then, to restriction of dietary carbohydrate in prescribing a diet is that the initial weight and water debt that is incurred will have to be repaid when carbohydrate is refed, as it eventually will be.

Recognition of the caloric value of a pound of body fat puts into perspective the reports of individuals who gain or lose 5 lb or more in a day. This must be a loss of fluid. Such changes are particularly evident when body fluid-retaining mechanisms are highly activated due to hormonal, emotional, medicinal, or dietary factors. Realization of this will help the dieter who has steadfastly maintained a 2- or 3-lb weekly weight loss when he finds, after a Thanksgiving indulgence, that he has gained back, in one meal, the weight lost during two weeks of dieting. He should be made to understand that resumption of the diet will result in nearly complete elimination of this excess fluid and leave him with only a minor shift in his weight-loss chart and a pleasant memory of a delicious meal.

Comprehension of these few basic facts makes rational the physician's relationship with his obese patient. Realistic goals can be set, and a practicable schedule prescribed. There is no single best weight-reduction formula. I feel that a balanced diet of 1,200 to 1,600 calories is one that is consistent with a long-range program on which any genuine effort to reduce weight must rest. Crash programs, while of temporary novelty interest, are insufficient. The addition of drugs to the program only serves to introduce artifactual and confusing features. In addition, drugs can be habituating and harmful. But most important of all, they serve to transfer the responsibility of dieting from the patient, where it must remain, to the pill bottle. If success in weight reduction is to be attained, the credit will belong to the individual and not the pill; conversely, if failure results, it is certainly not the fault of the pill.

Certainly, all the factors operative in human obesity are not fully understood; important work remains to be done in this field. However, knowledge of the scientific principles involved in weight reduction can offer greater opportunity for success



in this widespread problem. It is the physician's responsibility to assume an enlightened educative role in the therapy of human obesity.

This work was supported by Public Health Service research grant AM-08827 from the National Institute of Arthritis and Metabolic Diseases.

#### Generic and Trade Names of Drugs

Dextroamphetamine sulfate—*Dexedrine*.

Chlorothiazide—*Diuril*.

(The omitted figures and references may be seen in the original article.)

## HYPERPARATHYROID CRISIS

### A COLLECTIVE REVIEW

*LT W. A. J. MacLeod, MC USN, CAPT C. K. Holloway, MC USN,  
From the Department of Surgery, Naval Hospital, San Diego,  
California, Ann Surg 166(6):1012-1015, December 1967.*

Hyperparathyroid crisis is an infrequent occurrence in the otherwise chronic disease of hyperparathyroidism and represents a rapid progression of that process which, if left undisturbed, may pursue a fatal course. This disease process with its elevated serum calcium and progressive symptomatology has been variously termed parathormone intoxication, acute hyperparathyroidism, parathyrotoxicosis, parathyroid poisoning, and hyperparathyroid crisis.

In 1965, Payne and Fitchett reviewed the literature and, although recognizing a lack of generally accepted criteria upon which to base the diagnosis, listed 70 cases of hyperparathyroid crisis. Fifteen cases not included in their review and one additional case are reported in this paper.

#### Diagnosis

While any individual case of acute hyperparathyroidism may involve a large and confusing array of symptoms, particularly since the symptoms reflect multiple organ system involvement, it should be recognized that the presenting symptoms are indicative of hypercalcemia and do not distinguish any disease process, such as acute hyperparathyroidism, from any other disease, the result of which is an hypercalcemic state. Involved in the symptoms may be gastrointestinal, renal, neuromuscular and skeletal systems, as well as the central nervous system. Anorexia, nausea, vomiting, weight loss, constipation, diarrhea and abdominal pain are associated with gastrointestinal involvement, while polyuria, thirst, nocturia and dehydration may be related to renal

involvement. Back and extremity aches and pains, weakness, lethargy, and vasomotor instability are hypercalcemic symptoms of the neuromuscular and osseous systems. Hypercalcemia may affect the central nervous system with progression from lassitude to confusion, irritability, memory loss, decreased mental acuity, somnolence, stupor, and finally, coma.

Of some help in differentiating acute hyperparathyroidism from other hypercalcemic states are the occasional associated findings of peptic ulcer, pancreatitis, hypertension and renal stones. Anglem, in reviewing 69 cases, found either peptic ulcer or peptic ulcer-like symptoms in 30 percent, while gastrointestinal symptoms occurred in 63 percent of cases. Pancreatitis was reported by the same author in 11.5 percent of the cases surveyed. Lemann and Donatelli in 1964 reviewed 42 cases of hypercalcemic crisis due to acute hyperparathyroidism and found hypertension in nearly one third of that series. The same authors reported nephrolithiasis in about one half of the cases of fulminating hypercalcemia due to hyperparathyroidism.

The disease states which must be differentiated from hyperparathyroidism are many, including sarcoidosis, Paget's disease, hyperthyroidism, the milk-alkali (Burnett's) syndrome, immobilization, idiopathic hypercalcemia of infancy, hypervitaminosis D, and Addison's disease (and a similar, although iatrogenic condition, the steroid withdrawal syndrome) as well as cancers of such diverse tissues as breast, lung, renal, lymphoma, Hodgkin's disease, leukemia, and multiple myeloma.

Although the diagnosis of hyperparathyroidism may be suspected on the basis of symptoms alone,

a number of studies, including roentgenologic examinations, chemical analyses, and special diagnostic procedures are available and have been listed by Wilson as aiding in the establishment of a diagnosis of primary hyperparathyroidism. Often times the diagnosis of hyperparathyroid crisis cannot be delayed for these tests due to the fulminating course of the disease; and one must, therefore, depend on history, physical examination, and a few rapid, simple tests. The most useful single laboratory test is a serum calcium determination, all other tests of hyperparathyroidism are less constant. Even serum calcium levels may vary considerably, Henley and Smith *et al.*, reported instances with relatively normal calcium levels even though patients were manifestly in hypercalcemic crisis. (Smith and his group note that calcium levels may be relatively normal in patients with decreased serum proteins, while unmeasured ionized serum calcium, apparently the important factor, may be elevated. An additional consideration is that serum calcium levels may be normal or depressed with co-existent hyperparathyroidism and pancreatitis.)

Other studies which may be of value are ECG, in which there may be shortening of the Q-T interval and a nearly absent S-T segment, and an ophthalmologic examination for conjunctival and corneal lesions.

#### Case Report

A 76-year-old woman was admitted to the hospital on September 27, 1965. She had anorexia for the preceding two years, during which time she lost weight from 140 to 105 pounds, her weight at the time of admission. In July 1965, the patient became aware of increasing anorexia and dysphagia, and nausea after eating. In contrast to a long history of constipation, she began having as many as six loose stools a day. Infrequently during the year prior to admission, she had episodes of abdominal pain which remitted spontaneously. The patient had no headaches or polyuria, and there was no history of peptic ulcer disease or pancreatitis. She complained of weakness and of general malaise.

The patient was dehydrated and moved and spoke slowly, although she seemed oriented and alert. Blood pressure was 136/88, pulse 70, and temperature 36.4°C. There was a Grade III/IV systolic ejection murmur at the left sternal border, radiating to the apex and left axilla. The remainder of the examination was unremarkable.

Laboratory: Admission tests including serum bilirubin, CBC, reticulocyte count, electrolytes, urinalysis, BUN, alkaline phosphatase, SGOT, and blood glucose, were normal. Gastric analysis of 20 cc. of aspirate showed 24° of free HCl and 52° of total acidity.

BSP on October 4 was 8 percent retained. On October 5 serum phosphorus was 2.8 mg./100 ml. and serum calcium 18.8 mg./100 ml. On October 9 serum calcium was 16.8 mg./100 ml. with the remainder of the electrolytes normal. On October 11 serum calcium was 17.2 mg./100 ml. and on October 12, 19.6 mg./100 ml. On October 12 white blood count was 29,000 with a shift to the left; urine contained white and red blood cells too numerous to count and albumin; electrolytes: CO<sub>2</sub>—21 mEq./L., chlorides—90 mEq./L., sodium—125 mEq./L., and potassium—5.1 mEq./L. Blood drawn shortly before the patient's death had a serum calcium of 19.6 mg./100 ml.

A bone marrow biopsy showed normal cellularity with moderately increased numbers of eosinophils.

Roentgenograms of the skull and chest, and a barium enema were normal. Chest x-ray on October 12 revealed infiltrates in both upper lung fields.

Electrocardiograms at first showed a coronary nodal rhythm, occasional premature ventricular contractions and nonspecific ST segment and T-wave changes, then on October 12 supraventricular tachycardia, ST-T changes of digitalis effect and myocardial ischemia. QT intervals were normal in all tracings.

Shortly after admission, the patient became confused. Oral intake was poor, and intravenous fluids were given on September 30 with an initial gratifying response, in that the patient became more alert and less confused. This was only transitory, however, and she again became confused, progressing to a stupor on October 10. The first notation of elevated serum calcium was made on October 9 and the patient given Solu-Cortef.

On October 11 at surgical consultation a 2 x 3-cm. nodule was found in the left anterior cervical area and thought to be a parathyroid adenoma. The nodule was excised as an emergency procedure under local anesthesia, and shown to be a parathyroid adenoma from the area of the left inferior pole of the thyroid.

Six hours after operation, the patient's condition had not improved, and serum calcium level was 19.6 mg./100 ml. The patient continued to deteriorate.



Table 1.—Reported Cases of Hyperparathyroid Crisis (Since Payne and Fitchell)

Case	Author	Date (publ.)	Age, Sex	High Ca <sup>++</sup> (mg./ 100 ml.)	Low P (mg./ 100 ml.)	Opera- tion	Pathology	Outcome
71	Naik <i>et al.</i>	1963	45-M	19.5	—	No	Carcinoma	Fatal
72	Henley	1964	29-F	22.5	3.4	No	Adenoma	Fatal
73	Henley	1964	50-M	18.5	2.6	Yes	Adenoma	Survived
74	Henley	1964	62-F	18.0	4.8	No	Adenoma	Fatal
75	Henley	1964	75-M	17.8	4.6	Yes	Adenoma	Survived
76	Henley	1964	66-F	18.4	2.2	No	Adenoma	Fatal
77	Pringle and Smith	1964	38-M	20.0	2.1	Yes	Adenoma	Fatal
78	Pringle and Smith	1964	62-M	19.0	2.9	Yes	Adenoma	Fatal
79	Chodack <i>et al.</i>	1965	61-F	19.8	4.5	Yes	Adenoma	Survived
80	Chodack <i>et al.</i>	1965	63-F	19.3	5.4	No	Adenoma	Fatal
81	Kleppel <i>et al.</i>	1965	43-M	20.0	1.7	Yes	Adenomas, 2	Fatal
82	Kutner and Morton	1965	48-F	19.8	2.6	Yes	Adenoma	Survived
83	Kutner and Morton	1965	56-F	21.0	3.9	Yes	Adenoma	Survived
84	Schenker and Kullner	1965	30-F	—	—	No	Hyperplasia	Fatal
85	Anglem	1966	59-M	21.0	2.5	Yes	Adenomas, 3	Fatal
86	MacLeod and Holloway	1967	76-F	19.6	2.8	Yes	Adenoma	Fatal

ate and died 19 hours after operation with the serum calcium level unchanged.

At postmortem examination, no additional parathyroid adenomata were found. There was deposition of calcium in the renal tubules. Additional findings were bronchopneumonia, pulmonary edema, cholelithiasis, indolent chronic pancreatitis, mild atherosclerosis and a healed myocardial infarct.

This case is one of chronic hyperparathyroidism with progression to crisis at the time of hospital admission. The significance of elevated serum calcium levels coupled with rapidly progressive deterioration was not appreciated until too late. The patient was *in extremis* at the time of operation.

This case substantiates the premise of James and Richards that immobilization of the patient during hospitalization increases the hypercalcemic state with a resultant increase in the rate of deterioration.

#### Discussion

In Table 1 are case reports of hyperparathyroid crises found in the literature since the review by Payne and Fitchett. In this report, as in that of Payne and Fitchett, the criteria for inclusion have been rising serum calcium levels above 15 mg./100 ml.; rapidly progressive changes in a patient's general condition, especially when acute symptoms involved gastrointestinal, cardiovascular or central nervous systems; and rising blood urea nitrogen concentrations or other changes in renal function.

These two series total 86 cases and reveal the following data: Ages range from 5 to 77 years, with a median age of 51. The greatest incidence is during the three decades between 40 and 69 years, with

62 cases (72 percent), almost evenly divided between each of the three decades. Although hyperparathyroidism is more common in females than in males, by a ratio of approximately 2:1, the sex ratio of these 86 cases is very nearly 1:1, or 46 females to 40 males. Survivors numbered 34 patients, or nearly 40 percent, while there was a fatal outcome in 52 patients, or 60 percent. Of 45 patients undergoing operation, 33 survived—just over 38 percent of the total. Of those undergoing operation but not surviving, the majority were either *in extremis* at the time or had multiple adenomas, some of which were missed at the time of operation.

Of patients not operated upon, the outcome was invariably fatal, except in one case of a 5-year-old child in whom the hyperparathyroid crisis was precipitated during treatment for purpura with large doses of parathormone. The patient made a prompt recovery after cessation of treatment.

The pathologic lesions include: 67 parathyroid adenomas, seven instances of multiple adenomas, eight hyperplasias of the gland, three carcinomas, and one induced crisis.

Management of hyperparathyroid crisis may be divided into three phases: (1) preparation, during which medical management in the interim between diagnosis and operation may improve the clinical state of the patient; (2) surgical extirpation, since the only curvative measure known is removal of the hyperfunctioning parathyroid tissue; and (3) post-operative management. Such agents as sodium edetate, intravenous sodium citrate, sodium sulfate and sodium chloride infusions, or inorganic phosphate infusions have been recommended or employed

with varying degrees of success in medical treatment. However, because of the availability of the huge reserve of calcium in the adult skeleton, estimated by Lemann and Donatelli to be about 35,000 mEq. (as compared to the small extracellular calcium concentration, estimated to be about 50 mEq.), attempts to improve the clinical state by decreasing serum calcium levels by binding or removal may be ineffectual or only transient. Perhaps, as others have suggested, the only worthwhile preoperative preparations are adequate hydration and restoration of electrolyte balance.

Management after operation is essentially as for any postoperative parathyroid adenomas, except when the calcium levels fail to return to normal. The problem is then whether there is missed hyper-

functioning parathyroid tissue at the time of operation or renal insufficiency.

#### Conclusions

The diagnosis of hyperparathyroid crisis may be difficult but should be suspected in any instance of diffuse symptomatology involving gastrointestinal, cardiovascular, neuromuscular, skeletal, renal or central nervous systems and especially when a rising serum calcium level exceeds 15 mg./100 ml., blood urea nitrogen rises, and a patient's general condition rapidly deteriorates. Once the diagnosis is made, the need for emergency operation has been established; delay to further substantiate the diagnosis or to attempt to lower the hypercalcemia may be fatal.

(The references may be seen in the original article.)

## CLINICAL SEVERITY OF TETANUS IN NARCOTIC ADDICTS IN NEW YORK CITY

*Charles E. Cherubin, MD, New York, Arch Intern Med  
121(2):156-158, February 1968.*

Between January 1955 and July 1967, 42 cases of tetanus were treated at Metropolitan Hospital. All but four cases occurred in narcotic addicts. The majority of these have been Negro women (60 percent) from the Harlem area. The disease was severe and rapidly progressive; the case fatality rate was nearly 90 percent. Since 1955, the majority of cases of tetanus in New York City reported have been in addicts. The case fatality has been high. Subcutaneous injections appear to have been the site of injury for the majority. Particular therapeutic agents were less important in the outcome of the disease than tracheostomy care and bronchial toilet. A respiratory death was strongly suggested in the majority of cases. Tetanus is the single most difficult medical complication of drug addiction to treat.

Although, to the best of my knowledge, tetanus was first reported in association with narcotic addiction 90 years ago, it has only been during the past decade that drug addicts began to represent, in some areas, a significant part of the total number of

patients with tetanus. A recent survey of the epidemiology of tetanus in New York revealed that since 1955 the majority of cases have occurred in addicts. In Chicago addicts are known to constitute at least one half of the fatal cases of tetanus.

The present study describes the unique clinical features of a new form of "urban" or addict tetanus. The high frequency of Negro women, the relatively young age of the patients, and finally the strikingly high mortality which contrast with the usual picture of tetanus gives this the appearance of a "new disease." In particular, the study summarizes the experience with 42 cases of tetanus at Metropolitan Hospital, New York.

#### Clinical Material

Between 1955 and July 1967, 42 cases of tetanus were treated. Thirty-eight cases occurred in narcotic addicts and four in nonaddicts. Of the 42 clinical charts, one could not be located and several did not contain the complete record.

During the same period, 114 cases of tetanus were reported in New York City to the Bureau of Preventable Diseases. Three quarters of these cases (89 of the 114) were addicts. Of the addicts' cases,

Received for publication Sept 13, 1967; accepted Nov 8.  
From the Department of Medicine, Infectious Disease Service of Metropolitan Hospital, and the departments of preventive medicine and of medicine, New York Medical College, New York.  
Reprint requests to the Hospital Epidemiologist, Harlem Hospital Center, 138th St and Lenox Ave, New York 10037.



86 percent had been seen in a municipal hospital, 60 percent having been reported by the three large Manhattan hospitals of this type. The records of these three hospitals revealed that only 50 percent of their cases of tetanus had been reported. In the 12½-year period, 94 cases had actually been treated in these three hospitals and 90 percent of these cases had been addicts.

Two thirds of the addict patients seen at Metropolitan Hospital were women; and nearly all of these were Negro women while the nonaddict patients were all men. This appears to be changing. Since 1965, one half of the addict cases admitted to this hospital have been men. The addicts were also younger than the nonaddicts with a mean age of 31 years as compared with 45 years for the latter.

### Clinical Presentation

In nearly every addict case, abscesses or subcutaneous indurations or nodules were described. Twenty of the 30 cases at the Metropolitan Hospital in which this information was noted used the subcutaneous route of injection ("skin-popping") primarily; five were intravenous ("mainlining") users primarily, if not solely; and five used both methods. All 25 who used the subcutaneous route only, or in part, had multiple chronic abscesses on the thighs and occasionally over the deltoids. Fluctuant abscesses were found, however, in only seven. Four of the five cases who used "mainlining" entirely had an evident cellulitis or abscess on admission.

### Symptoms

The first symptom of the majority of tetanus patients was stiffness or pain in the neck or back (Table 1). Trismus was noted usually several hours afterward. The interval between the onset of symptoms and admission to the hospital was very short

Table 1.—First and second symptoms of tetanus \*

	No.	% †
First Symptom		
Trismus	8	27
Stiff or painful neck	11	37
Stiff or painful back	7	23
Chest pain	2	7
Difficulty in eating or chewing	2	7
Second Symptom		
Trismus	10	35
Stiff or painful neck	5	17
Stiff or painful back	8	23
Chest pain	0	0
Difficulty in eating or chewing	6	21
Headache	1	4

\* All patients at the Metropolitan Hospital, 1955 to July 1967.

† Percent to nearest whole number.

Table 2.—Interval of symptoms prior to admission, between admission and tetanospasm, between admission and death, and case fatality rate

	Addicts		Nonaddicts	
	No.	%	No.	%
Symptom prior to admission				
<1 day	14	41		0
1 day	15	44	1	25
2 days	3	9	2 *	50
3 + days	2	6	1	25
Admission prior to tetanospasm				
On admission	10	36	1	25
<1 day	7	25	0	0
1 day	3	11	1	25
2 days	6	21	0	0
3 + days	2	7	1	25
Never	0	0	1	25
Admission prior to death of fatal cases				
<1 day	3	9	0	0
1-2 days	10	31	0	0
3-4 days	7	22	0	0
5-8 days	11	35	2	50
>8 days	1	3	2	50
Case fatality rate		87		50

\* One patient in the hospital at the time tetanus developed—admission interval estimated as the time from onset of symptoms to clinical recognition of the disease.

for the addicts. Twenty-nine of the 34 cases were hospitalized within 24 hours or less (Table 2). Only two patients remained outside the hospital for more than two days—actually these patients had been trying to be admitted for several days.

For the City as a whole, addicts were hospitalized several days sooner after the onset of symptoms than nonaddicts and this difference was statistically significant.

### Hospital Course

The disease in addicts develops with great rapidity. All addict cases at this hospital had generalized tetanospasm within three days after admission. A majority had tetanospasm and opisthotonos within 24 hours (Table 2). Two thirds of the deaths in the addict group occurred within the first four days after admission, and only one patient died after the eighth day (Table 2).

A comparison between the addict and the nonaddict cases of tetanus for the City as a whole showed a significantly shorter hospital stay prior to death for addicts, with nonaddicts dying usually after a prolonged period of hospitalization. This was also noted at Metropolitan Hospital although the number of nonaddict cases was small. The fatality rate at Metropolitan Hospital was 87 percent for addicts and 38 percent for nonaddicts.

Patel and Joag have reported from India that the most severe disease and highest mortality occur with puncture wounds. This is consistent with the above findings and may mean that puncture wounds—a characteristic that all addict cases share—are more favorable to toxin production and absorption than other types of wounds.

#### Therapy and Complications

Large doses of antibiotics (usually penicillin and tetracycline), a variety of sedatives, and, until recently, extremely large doses of antitoxin (50,000 to 1,000,000 units of tetanus antitoxin) were universal in the therapy of this disease in New York. A tracheostomy was performed in nearly all instances, the only exceptions being some mild non-addict cases. Neuromuscular blocking agents and intravenous barbiturate anesthesia were used in many patients but could not be evaluated as other factors in patient care seemed of more importance. Clostridia were never cultured at the Metropolitan Hospital from the suspected area of infection. This was similarly the case in the records reviewed at other hospitals.

At the Metropolitan Hospital there were two immediate reactions to antitoxin; and of the six cases surviving up to one week who had been given massive antitoxin therapy, three developed a serum-sickness-like illness.

Tracheostomy, especially as an emergency procedure under adverse conditions, was in itself an important source of complication. Respiratory obstruction, local infection, pneumonia, and inspissation of secretions were noted. Fever and leukocytosis were, with four exceptions, noted only after tracheostomy. These four cases included three patients with extensive cellulitis and one with a bronchopneumonia present on admission. Fever, 102 to 104 F (37.9 to 38 C), occurred in conjunction with pulmonary infiltrates, thus implying secondary sepsis and not the disease itself. Blood cultures were frequently positive at this time. At autopsy, all cases showed some bronchopneumonia; and in two of the last seven deaths, it was extensive, involving three or more lobes.

Death was usually sudden; and when observed, it was preceded by convulsions and apnea. Respira-

tory impairment was uniformly implicated, either due to obstruction of the airways, spasm or fatigue of the respiratory muscles, inadequate mechanical respiratory assistance systems, or a diffuse pneumonia. The time of death was the late evening or early morning in 80 percent, and 80 percent of the patients were clearly unattended on the basis of the record at the time of death.

In the patients in this series, a respiratory death due to retained secretions or inadequate ventilatory assistance was strongly suggested. The early death, the time (evening or early morning), and the nurses and physicians' notes argue that this difficult and drawn out therapeutic problem may have been poorly handled even during the initial period. When continuous nursing care was temporarily provided, marked worsening of the patients' clinical condition or death followed within 24 hours of the cessation of this coverage. This argues that it is not a particular agent or a dosage schedule which is of paramount importance but rather the meticulous nursing care, especially tracheostomy care and bronchial toilet, which make for therapeutic success.

It follows that these patients should be treated in an intensive care unit with continuity of medical and nursing personnel. Severe tetanus requires a surgical plane of anesthesia or curarization and, therefore, tracheostomy, continuous mechanical respiratory assistance, blood gas and ventilatory analysis, intravenous fluid, and continuous nursing for periods of at least two weeks. The cost is enormous, and obviously it would be preferable to prevent the disease by creating immunization programs in all institutions and agencies that have contact with addicts. Until this occurs, there is a clear need to improve our methods of treating these patients.

The disease is a relatively uncommon one, but a unique epidemiologic situation in upper Manhattan has increased the incidence of severe tetanus to the point that it has become a significant diagnostic and therapeutic problem.

#### Generic and Trade Names of Drug

Tetracycline—*Achromycin*, *Panmycin*, *Polycycline*/Formerly, *Tretracyn*.

(The references may be seen in the original article.)



# MEDICAL ABSTRACTS

## THE TPI AND FTA-ABS TESTS IN TREATED LATE SYPHILIS

W. G. Atwood, MD, et al., *JAMA*  
203(8):549-551, Feb 19, 1968.

Sixty-seven patients who had been diagnosed and treated 13 or more years ago for latent or late syphilis were retested with use of several serological tests for syphilis. At the time of original diagnosis, all patients had been reactive in cardiolipin reagin tests and in the *Treponema pallidum* immobilization (TPI) test. It was found that 73% of patients were still reactive in one or more cardiolipin reagin tests and that 90% had retained TPI reactivity. In the newer fluorescent treponemal antibody-absorption (FTA-ABS) test, 98% were reactive. These results indicate that the FTA-ABS test is more sensitive than the TPI test. *Neither the FTA nor the TPI test, as presently performed, may be used as an index of therapeutic response, since both tests show reactivity 13 or more years after presumably adequate treatment.*

## THE BIOLOGY OF MYOCARDIAL INFARCTION

Gunnar Björck, MD FRCP, *Circulation*  
XXXVII(6):1071-1085, June 1968.

Myocardial infarction is a dreaded companion of the civilization of our time. The "heart attack," the coronary thrombosis, the myocardial infarction lurk behind the corner, striking strangers, patients, friends, and ourselves. The toll taken by this single "disease" in many hospitals equals or even exceeds that from almost all other diseases together. Must it be so? This is the question many physicians, and the lay public, are asking themselves today.

Identification of some areas where our knowledge is particularly deficient is stressed. We must concentrate our efforts on reevaluating practices and procedures that have brought both the greatest success and the worst failures, at the same time that we ask ourselves what goals could be considered realistic.

If myocardial infarction is the evil of our time, what does this mean in a greater biological context—in the evolution of human life and endeavor as viewed in perspective? Are we dealing with a "disease" in the restricted sense of the word, or are we dealing with a way of life and a consequent mode of death? If so, what can be done to achieve the goals of health as defined by the World Health Organization? In what terrain are the forces to be assembled and the battle to be fought—and by whom.

## MORTALITY AND HARDNESS OF LOCAL WATER-SUPPLIES

M. D. Crawford, MD Glasg, et al.,  
*Lancet* I(7547):827-831, Apr 20, 1968.

In the sixty-one county boroughs of England and Wales with population 80,000 or over in 1961, the harder the local drinking-water and the more calcium it contained the lower was the death-rate in middle and early old age; this was particularly so for cardiovascular and, to a lesser extent, bronchitis mortality, confirming findings relating to the period around 1951. No evidence was obtained that water hardness was reflecting some other environmental factor. A multiple regression study showed that water calcium makes a substantial and highly significant contribution to the variance of the cardiovascular death-rate, between the sixty-one towns, after allowing for environmental factors. Chemical studies of trace elements in water from consumers' taps showed none at a concentration which could be considered toxic either in towns with very soft or with very hard water. Apart from the main minerals—calcium, magnesium, and sodium—only six elements showed consistent differences between the soft and hard waters—manganese and aluminium (higher concentrations in soft waters), and boron, iodine, fluorine, and silica (higher concentrations in hard waters). There is no acceptable explanation at present for the associations found between water hardness and mortality. There is, however, urgent need for incidence and prevalence studies, and detailed investigation of the problem by chemists.

## EXERTIONAL RHABDOMYOLYSIS IN NAVAL OFFICER CANDIDATES

Raphael F. Smith, MD, *Arch Intern Med*  
121(4):313-319, Apr 1968.

Eight young men undergoing heavy repetitive exertion manifested a syndrome consisting of severe myalgia, myoglobinuria, elevated serum levels of enzymes of muscle cell origin, and impaired muscle function. Stress testing after recovery did not reproduce this syndrome. Subclinical rhabdomyolysis was detected in a prospectively selected group of 38 young naval officer candidates. Rarity of overt rhabdomyolysis in a large homogeneous population of men exposed to similar exercise stress conditions in preflight training, and negatively skewed distribution of serum enzyme values in a sample of this population suggest that rhabdomyolysis causing impaired muscle function occurs after prolonged calisthenics in certain predisposed individuals rather than in all poorly conditioned men. Prior physical conditioning lessened the probability of this occurrence, supporting the recommendation for a graduated physical training program.

## CARCINOMA OF THE BREAST

M. Haimov, MD, et al., *Amer J Surg*  
115(3):341-348, Mar 1968.

Seven hundred fifty-seven cases of carcinoma of the breast in women seen on the ward service of The Mount Sinai Hospital from 1933 to 1965 are reported. Five hundred forty-two of these patients underwent radical mastectomy and the long-term follow-up study of these patients is presented.

The over-all five and ten year survival rates were 51 and 41.7 percent, respectively. The five and ten year survival rates for stage I carcinoma was 64.4 and 54.1 percent, for stage II carcinoma 49.6 and 27.9 percent, and for stage III carcinoma 15 and 12 percent. These results indicate that radical mastectomy is effective in treating patients with stage I and II carcinoma of the breast but is of no value in patients with stage III carcinoma in whom survival after radical mastectomy does not differ from that in untreated patients with carcinoma of the breast.

## DENTAL SECTION

### WHAT ABOUT A VACCINE FOR THE PREVENTION OF DENTAL CARIES?

Gordon H. Rovelstad, *Dent Abs*  
13(7):401, July 1968.

A vaccine to prevent dental caries is a possibility and is worthy of every bit of effort that can be mustered to support it.

It has been proved that bacteria are essential to the development of caries in experimental animals. Characteristic streptococci have been found to be infectious and transmissible in producing caries in experimental animals.

In recent years, the Navy has conducted a study in progress in which naval recruits having perfect teeth are selected. Opportunities for these men to serve one year of duty at Great Lakes have been offered to them, during which time they have become subjects of extensive dental studies along with, and in addition to, their regular duties. One hundred and forty-five such recruits have been included in these studies. Only 37% of the 145 came from areas where optimum amounts of fluoride are known to be present in the water supply. Of the 145, more than half developed caries while in the study.

From those who have developed caries, many different isolates of streptococci were obtained by Shklair (1967). These streptococci have been placed in four groups biochemically. To date, one of these streptococci has been inoculated into germ-free rats and found to produce caries. Tentatively, Koch's postulates can be said to have been satisfied on these initial experiments with caries in humans.

This suggests the simplest of mechanisms of disease, that of bacterial infection. Previously disease-free young men, on arriving at Great Lakes and mixing with many other young men having caries, not only develop caries but demonstrate the presence in increasing numbers of a form of streptococci known to produce the disease. Further studies have shown that those caries-free subjects who remained free from caries during the year of observation period, had a higher antibody titer to some cariogenic microorganisms than a group of caries-active subjects. Experimental evidence has been reported recently (Fox and others, 1966) indicating high antibody titers in humans as a result of the administration of a vaccine prepared from the "M" proteins of at least three types of strep-

tococci. Thus the vaccine concept based on "M" protein antigens has been found feasible.

Recently Wagner (1967) has reported that rats inoculated orally with *Streptococcus faecalis* and parenterally immunized with the homologous bacteria, demonstrated the virtual elimination of caries as compared with the nonimmunized control animals. If recent findings are substantiated by investigations in progress, it seems that a vaccine to prevent caries is a possibility.

(Rovelstad, Gordon H., Naval Dental Research Institute, Great Lakes, Ill. What about a vaccine for the prevention of dental caries? J Amer Coll Dent 35:74-81, Jan 1968.)

Copyright by the American Dental Association. Reprinted by permission.

#### EARLY DIAGNOSIS OF ORAL CANCER

Richard W. Tiecke, Chicago, Ill., Geriatrics  
23(2):114-117, Feb 1968.

Early diagnosis of intraoral carcinoma is of utmost importance because of its low survival rate and unfortunate alternatives faced by the patient when it is not discovered early. These problems relate chiefly to facial deformity and impaired function of oral structures which often follow surgical removal of large intraoral tumors. The five-year survival rate of intraoral carcinoma is lower than that for carcinoma of the skin, uterus, breast, colon and rectum. Intraoral carcinoma can be cured when discovered and treated while in an early stage of

development. Such lesions are often overlooked because of their small size and lack of subjective symptoms and because their appearance does not correspond to the changes generally associated with cancer's seven warning signals. The warning signals of intraoral carcinoma are: (1) a swelling or growth in the palate, tongue, buccal mucosa, floor of the mouth, or gingiva, (2) asymmetry of the oral structures of the face, (3) a persisting red spot in the oral mucosa, (4) a persisting white patch in the oral mucosa, (5) an unhealed ulcer in the oral mucosa, (6) difficulty in swallowing, (7) radiograph of jaws showing irregular, ill-defined radiolucent area of bone with possible resorption of roots of the teeth, or (8) a combination of any of these signs.

A thorough examination of the soft and hard structures of the oral cavity is the major procedure in finding early oral carcinoma. Biopsy is the most important and reliable method for obtaining a definitive diagnosis and is indicated when malignancy is suspected or a lesion fails to respond to therapy within five days to a week.

Oral cytology may be used to aid in the interpretation of small unsuspected abnormal areas on the oral mucosa. However, it must be noted that it is intended as an adjunct to biopsy and not a replacement.

(Abstracted by: CAPT George H. Green, DC USN.)

## PERSONNEL AND PROFESSIONAL NOTES

### APPLICATION FOR ADVANCED TRAINING

Dental officers intending to submit applications for assignment to long courses of instruction commencing in Fiscal Year 1970 are encouraged to do so at the earliest possible date in accordance with MANMED article 6-130. This includes applications for graduate/postgraduate courses at the Naval Dental School, second and third year level of training (residency type), postdoctoral fellowships and long courses at civilian universities.

The Dental Training Committee in the Bureau of Medicine and Surgery will convene in October 1968 to consider applications for long courses at civilian universities in accordance with BUMEDNOTE 1520 of 31 May 1968, in order to provide the approved trainee with sufficient time to meet university deadlines for enrollment. The committee will reconvene in early January 1969 to consider late applications for long courses at civilian universities and all other

applications for advanced training commencing in Fiscal Year 1970.

Currently, the advanced training program with the greatest percent of opportunity is the postdoctoral fellowship program in Periodontology. Officers submitting applications for a long course of instruction in Orthodontics are encouraged to include a second choice of advanced training because of the limited number that can be approved for orthodontic training.

NAVMED P-5093 of 1 July 1968 has been distributed to all major naval activities. This publication provides information for all educational programs available to dental officers and lists detailed curricula for the major courses presented by the Naval Dental School. The increasingly higher professional capability of dental officers may, basically, be attributed to the Naval Dental Corps' educational programs.



## APPLICATIONS FOR CLASS "C" PROSTHETIC AND REPAIR SCHOOLS

The waiting list of eligible candidates desiring assignment to the Class "C" Prosthetic and Repair schools has been depleted. Qualified personnel desiring either of these courses are encouraged to submit requests in accordance with BUMEDINST 1500.9B, and to indicate school preferences in their rotation data cards.

Beginning with the Class "C" Prosthetic course which convened on 3 June 1968, fixed partial denture procedures have been added to the curriculum. To provide the time required for this extra material, the course has been lengthened from 26 to 34 weeks.

## FIVE-YEAR EQUIPMENT REPLACEMENT PROGRAM

The third increment of the Five-Year Equipment Replacement Program will most likely be implemented on an austere basis, due to funding limitations throughout the Navy. It is, therefore, imperative that the dental officers at activities not under BUMED support stress the importance of this program to their respective commanding officer. The Surgeon General has requested support for this program from all Bureau Chiefs, Systems Commanders, and the Commandant of the Marine Corps.

# NURSE CORPS SECTION

## REPORT REGARDING COLOR CODING ON INDIVIDUAL DOSE NARCOTIC PACKAGES

The pharmacy committee at one of the large naval hospitals recently submitted to the commanding officer a suggestion that narcotic dose packages be color coded. At the present time all boxes are of the same color and print. The Assistant for Materiel, Code 32-1, then requested the opinions of nurses at ninety-two medical facilities. Forty-nine were returned representing the opinions of 1,314 nurses. Of this number 725 were in favor of color coding and 589 were against the system.

Some of the comments from the affirmative group were:

1. Color coding would facilitate locating narcotic in locker.
2. It would aid in identification of the narcotic.
3. Provide an additional method of checking narcotic and dosage.

Comments from the negative group included:

1. It would tend to make identification by color more or less automatic resulting in carelessness in reading labels.

2. Some nurses might be color blind.

Other opinions expressed were:

1. Color coding should be confined to identifying the drugs only, not the strength of the same drug.

2. The name and dosage should be printed in large letters on the end of the box.

3. In addition to the use of color, a clear plastic packaging would allow for rapid counting without having to handle contents.

## INFECTION SURVEILLANCE NURSE AT NAVAL HOSPITAL, OAKLAND

LCDR Gladys Madsen, NC USN, has been appointed to fill a new position, Infection Surveillance Nurse at Oak Knoll. She will be responsible to, and the direct representative of the Chief of Nursing Service.

In preparation for her work, Miss Madsen spent a week at Kaiser Foundation Hospital observing the activities of their infections control program. She also attended meetings at Stanford University Hospital, where there is a nurse assigned to this specialty.

The infection surveillance nurse's responsibilities will include supervising and implementing the regulations and procedures recommended by the Infection Control Committee. She will report all known infections to the Chief of Nursing Service, and to the Chairman, Inspection Control Committee. In addition, she will confer with the doctors on the assignment of patients requiring isolation and inform and teach hospital workers in the proper handling of the patient and his environment.

In her new capacity, Miss Madsen will work with the Hospital Sanitation Officer and the Chief, Pre-

ventive Medicine in an attempt to control environmental sanitation by frequent sampling of the hospital areas where infections or contamination may be considered significant.

Since the problem of infection in hospitals persists, every avenue should be tried in an attempt to reach a solution. The Infection Surveillance Nurse may discover some of the answers.

## PREVENTIVE MEDICINE SECTION

### INFLUENZA—HONG KONG

An epidemic of influenza, in an estimated 300,000 persons in Hong Kong has been reported. First cases commenced on 13 July 1968 with a rapid increase in incidence reaching a peak on 25-26 July 1968. The disease has been clinically mild with symptoms lasting from 3-4 days. Deaths have been few in number and have occurred primarily in the very young and the aged.

Strains of virus have been isolated on primary cynomolgous monkey cell culture. All have been identified as type A<sub>2</sub> influenza by hemagglutination-inhibition tests. Serologic studies of patients are in progress.

American residents have been affected. About 30% of the staff at the American Consulate have experienced influenza-like illness during this epidemic. There has been no disruption of American tourist traffic.

In view of this outbreak, on 2 August 1968 the Bureau of Medicine and Surgery alerted Commander-in-Chief, Pacific Fleet, a Pacific Fleet Type Commanders, the U.S. Navy Preventive Medicine Unit No. 5 and U.S. Navy Preventive Medicine Unit No. 6, and other interested activities recommending annual influenza vaccine program begin as soon as possible for units assigned to the Seventh Fleet. The Commander-in-Chief, Pacific Fleet has implemented the early influenza vaccine program throughout the Pacific Ocean area by message.—PrevMedDiv, BuMed.

### 32nd ANNUAL EDUCATIONAL CONFERENCE ON ENVIRONMENTAL HEALTH

LT E. E. Jenkins, MSC USNR, and ENS J. D. Blaylock, MSC USNR, Environmental Sanitation Section (Code 7223), Preventive Medicine Division, Bureau of Medicine and Surgery, Washington, D.C. attended the 32nd Annual Educational Conference on Environmental Health, with guest speakers from

major environmental health areas which was held at the Sheraton-Park Hotel, Washington, D.C., June 23-28.

Sponsored by the National Association of Sanitarians, approximately 1,000 persons attended the national meeting on air and water pollution, noise abatement, health administration, food protection, housing and urban development, aerospace environments, hospital sanitation, microbiology, comprehensive health planning, accidental injury, health research, and education in environmental health.

Keynote speaker for the five-day event was Dr. Philip R. Lee, Assistant Secretary for Health and Scientific Affairs. Other special speakers included Dr. Rene Dubos of the Rockefeller University, Senator Ralph W. Yarborough of Texas; Dr. A. R. Slonim, Biomedical Laboratory, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base; Herbert H. Jones, Assistant Chief, National Noise Study Program; Dr. Carruth Wagner, Assistant Surgeon General and Chief, Bureau of Health Services, U.S. Public Health Service and James A. Anderegg, Assistant Director, National Center for Air Pollution.

Topical programs were sponsored by the National Center for Urban and Industrial Health, National Communicable Disease Center, National Institutes of Health and various schools of environmental health.

The National Association of Sanitarians is a 10,000 member association with headquarters in Denver, Colorado. According to the Association's Executive Director, Nicholas Pohlit, M.P.H., R.S., the Association experienced a dynamic conference because of the interprofessional and multidisciplinary program, one of first national meetings featuring speakers from many major fields of environmental health.

During the conference, both Mr. Jenkins and Mr. Blaylock were instrumental in the formation of the



"Uniformed Services Association of Sanitarians", which is a professional association of members of the National Association of Sanitarians on active duty in the Army, Navy, Air Force, Public Health Service, and other uniformed services.

Mr. Jenkins was elected Chairman-President and Mr. Blaylock was elected Secretary at the first meeting of the Uniformed Services Association of Sanitarians held on June 27 at the Sheraton-Park Hotel.—PrevMedDiv, BuMed.

## OUTBREAK OF TUBERCULOSIS — BUFFALO, NEW YORK

*USDHEW PHS NCDC Wkly Rep*  
17(29):270-271, July 20, 1968.

On 11 Jan 1968, a 32-year-old woman in Buffalo, New York, was found to have far advanced pulmonary tuberculosis by chest X-ray examination. Microscopic examination and cultures of her sputum were subsequently found positive for *Mycobacterium tuberculosis*.

Since 13 Sept 1967 the woman had been employed as a teacher's assistant in 2 classes (1 morning and 1 afternoon), located in a church building. She was in close contact with the 26 students, ages 3-5, in these 2 classes for 2½ hours each day while she supervised their play and teaching activities and helped them with their outdoor clothing. She had contact with 29 other students in an adjoining classroom because she frequently led her students through this room to the single restroom, used by both classes. The woman aided all 55 students with their meals. There was limited ventilation in both rooms because windows were closed during the cold weather.

The woman left her employment in Dec 1967, because of her illness. After tuberculosis was diagnosed in this woman, all 55 students, 9 adult school personnel, 8 parents and siblings of the school children, and 4 church employees were tuberculin tested on 26 January. An additional 21 close contacts and 14 casual contacts outside the school were tuberculin tested within the following 3 weeks. The Mantoux method with 5 tuberculin units of PPD was used and 10 mm of induration was considered a positive reaction. All students, both teachers, and the other teacher's assistant were considered close contacts to the woman. Her close contacts outside the school either lived in her household or lived elsewhere but had a similar degree of contact. All others with a significant contact were considered her casual contacts including the remaining 7 adult school personnel.

Of the 111 contacts of this woman, 28 had a positive reaction. Based on both a positive tuberculin test and chest X-ray evidence of enlarged hilar lymph nodes, 8 new active cases of primary tuberculosis were identified. Of these, 2 were documented tuberculin converters within the previous year; the other 6 had no record of a previous test. There were 3 other documented tuberculin converters with negative chest X-rays found on initial testing and 1 additional converter with a negative X-ray found on repeat testing 8 weeks later. Three of these 6 converters were under 5 years of age. Primary tuberculosis, the activity of which could not be determined at the initial examination, was diagnosed in an additional 4 contacts, and 12 others had inactive or probably inactive tuberculosis. No other converters were identified on retesting in May of the negative contacts although 23 of the 83 negative contacts were not available for reexamination.

The closeness of contact appeared to be related to the incidence of new infection in this outbreak. All 8 active primary cases were considered close contacts as were 2 of the converters without active disease. Four of the active cases were students in the index case's classroom, 1 was a student in the adjoining classroom, and 3 were her own children. Based on available attendance records, the duration of contact did not seem to be a factor in the outbreak. Each of the 4 students with active primary tuberculosis in the source case's room had an average of 142 cumulative hours of contact (range 118-162) and the case in the adjoining room had only 36 hours of contact, while each of the 21 tuberculin-negative students had an average of 148 cumulative hours of contact (range 87.5-180 hours).

It is of interest to note that the index case in this outbreak failed to submit to chest X-ray prior to beginning her teaching duties.

## PARATHION POISONING—TEXAS

*USDHEW PHS NCDC Morb & Mort Wkly Rep* 17(28):263, July 13, 1968.

On 13 June 1968, 23 cotton workers near Santa Rosa, Texas, were poisoned with the chemical parathion (O, O-dimethyl O-(p-nitrophenyl) phosphorothioate). Initial symptoms were nausea, vomiting, sweating, and extreme weakness, and 2 patients developed acute pulmonary edema. Onset of symptoms in all cases was about 2½ hours after the workers entered a field that had been sprayed with a combination of methyl and ethyl parathion the



night before. Of the 23 patients, 13 required hospitalization and 10 were treated as outpatients.

The patients were initially treated with 2 mgm atropine, intravenously, and 2 PAM (2-Pyridine aldoxime methochloride [or pralidoxime chloride].) In addition to treatment, immediate steps were taken to decontaminate the patients by removing their clothing and washing their skin to prevent further absorption of the parathion. Serum cholinesterase activity (which is depressed in organic phosphate poisonings) was determined on all patients by the Caraway method (Caraway, T.: Photometric Determination of Serum Cholinesterase Activity, *Amer J Clin Path* 26:945-955, 1956). The normal range for serum cholinesterase activity by this method is 65-100 units per ml. The values obtained for the hospitalized patients ranged from 2-8 units per ml and for the outpatients from 30-60 units per ml.

Within 3 days, all patients had completely recovered and were discharged from the hospital. Follow-up treatment for all 23 patients included atropine tablets in sufficient quantities to maintain a dry mouth and daily observation by the local physician.

On 12 June the cotton field had been sprayed with parathion. Because of a heavy dew that evening, considerable moisture was present on the cotton plants the following day. Because of this moisture and the height of the cotton plants (approximately 3½ feet), the workers' clothing was thoroughly soaked soon after work started in the field. These factors contributed to increased exposure to the parathion. All 23 workers were local residents, and most of them had worked for the cotton field owner for several years and had worked with parathion in the past without any adverse effects.

## RABIES

J. R. Held, E. S. Tierkel, and J. H. Steele, *Rabies in man and animals in the United States, 1946-65. Public Health Rep* 82(11):1009-1018, 1967 and *Trop Dis Bull* 65(5):613-614, May 1968.

In 1946 a national rabies control program was established in the United States and the epidemiological characteristics of rabies in man and animals during the first 20 years are reviewed. By far the highest incidence of the disease among domesticated animals is in dogs, and among wild animals in foxes and skunks; in 1965 the disease was reported in all but 3 states, Delaware, Nevada and Hawaii; the disease has never been reported in Hawaii.

There were 8,384 cases in dogs in 1946; 412 cases in 1965. The factors for the decline are considered to be widespread immunization and greater control of stray dogs, with more public health information. Rabies has also been reported in cattle, sheep, pigs, goats and horses but these animals are not likely to be important to maintaining the disease. From 1946-1960, there was an overall decrease from 10,883 cases to 3,457.

Rabies in skunks is a problem especially in the Great Plains states and California, whereas in foxes it is primarily a problem in the southeast and the Gulf states extending into the State of New York. Patterns change; Texas was once an area of fox rabies and latterly an area of skunk rabies. Bats and racoons are also important. Since 1953 rabies virus has been isolated from bats in all states except Alaska, Hawaii and Rhode Island; there is evidence that they transmit the virus by aerosols as well as by biting.

During 1946-65, 236 deaths from rabies were reported in man; there was a general decline from 33 in 1946 to 1 each in 1963 and 1964 and 2 cases in 1965. The greatest number occurred in the southern states and may be a reflection of urban epidemics in dogs which occurred early in the period under review. The species of animal responsible was known in 149 cases and of these, dogs were responsible for 122, cats for 9, foxes for 7, skunks for 6 and bats for 5. Of the 236 cases, 165 were in males and 71 in females and of 205 of known age a little over half were in children aged less than 15 years. The length of illness, where known, varied from 1 to 20 days with a median of 4 days; the period of incubation varied from 6 to 270 days with a median of 37 days (an exceptional case, not included in these figures, occurred in West Virginia with a reported incubation period of 23 months, and in this case there is the possibility of a second exposure to infection after prophylactics had been given). There is some evidence that immunoprophylactic treatment after exposure prevented cases which would have had longer periods of incubation; those with severe exposures had, in general, shorter periods of incubation. Although nervous tissue vaccine and duck embryo vaccine were used there is no evidence that nervous tissue vaccine is more or less effective than duck embryo vaccine. There is, however, a suggestion that hyperimmune serum, when given in addition to a vaccine, may interfere with the antigenic effect of a vaccine unless booster doses of vaccine are subsequently administered. Details are shown in 6 tables and 4 figures.

## CONTRIBUTIONS OF PESTICIDES OUTWEIGH HEALTH HAZARDS

*Arthur L. Van Duser, MD, Wisconsin Health*  
18(6):3-4, 27-29, 1968.

Synthetic pesticide agents have had rapid growth in usage and volume, without comparable growth in knowledge of their effect on the health of human beings.

Within 20 years after the introduction of chlorinated hydrocarbons the United States was producing synthetic organic pesticides at an annual rate of 700 million pounds, predominately for domestic consumption. Current literature suggests that 60,000 registered products exist and that at least 200 of them are high in importance in terms of volume and toxicity. Chemical pesticides may be placed in 4 major groups:

(1) Chlorinated hydrocarbons, such as DDT, dieldrin, aldrin, toxaphene, lindane, methoxychlor, chlordane, heptachlor, 2, 4-D, and 2, 4, 5-T.

(2) Organic phosphorus compounds, such as parathion, malathion, phosdrin, diazinon, bidrin, and TEPP.

(3) Other organic compounds, such as dinitrophenols, carbamates, organic sulfurs and mercurials, pyrethrum, rotenone, nicotine, strychnine and anti-coagulants such as warfarin.

(4) Inorganic and mixed substances, such as copper sulfate, arsenate of lead, calcium arsenate, compounds of chlorine and fluorine, thallium sulfate, sodium fluoracetate, zinc phosphide and mercurials.

Chlorinated hydrocarbons and some of the inorganic compounds tend to degrade slowly and leave long or relatively long residuals. In human toxicity the chlorinated hydrocarbons as a group rank relatively low. But one should be constantly aware that within a group there are agents of low and of high toxicity for humans. For example, DDT versus aldrin in the chlorinated hydrocarbons, malathion versus parathion in the organic phosphorus group and pyrethrum versus nicotine in the other organic agents. Nicotine is very toxic to humans, animal, and birdlife. One or two drops of nicotine in the oral cavity of a dog may be lethal, and birds can succumb to an inhalation of nicotine vapors.

Toxicity + Exposure = Hazard

The extent of the hazard associated with the use of pesticides is determined primarily by the toxicity of the compound and the degree of exposure. The rates of body entry through skin, inhalation, and oral routes vary greatly among pesticides. The rates are also modified considerably by solvents, formulations, concentrations, temperatures, techniques and methods of use. Thus it is very important that workers and household users always adhere to all safety regulations prescribed for each compound and use, or they will be risking the serious results of having one safety door closed and one open. In pesticide poisonings among the general public, the oral route is involved in at least 80% of the time, dermal and inhalation exposure routes are of relatively more importance to industrial workers than to the general public.

### Pesticides Research Tissues Through Foods

Chlorinated hydrocarbons are being found in human tissue of all ages and in many parts of the world. Prior to 1942, DDT was not demonstrable in human fat tissue, but by the early 1950's numerous reports were showing levels of 5 ppm. Generally pesticide levels in industrial workers are about 3 times as high as in the general public. The bulk of pesticides reaching human tissues get there through repetitive food ingestion. Some pesticides are rapidly altered, destroyed and excreted by the body. Others persist and accumulate and may reach toxic levels. With DDT and DDE being used as the indicators, it is estimated that nearly 60% of the ingested food pesticides are from meats, seafoods and eggs, 15% from vegetables, 10% from dairy products other than milk, 3% from milk, 3% from cereals, and 10% from other foods.

### Pesticides Reduce Starvation, Food Costs

The more significant beneficial health effects from pesticides are very large in social value, readily apparent, but not always, or fully recognized. The use of pesticides in food production has prevented

Presented at the 22nd Annual Wisconsin Pest Control Conference with Industry, Sponsored by the College of Agriculture.

and reduced famine and starvation in large segments of the world population, and has greatly reduced food costs. Better world nutrition has also meant better world health with greater resistance to common disease morbidity and mortality. The use of insecticides to destroy insect vectors and thus control or eradicate many of the infectious diseases has reduced human illness by hundreds of millions of cases. Some of these diseases include: malaria, yellow fever, typhus fever, relapsing fever, virus encephalitis, rickettsialpox, trench fever, Rocky Mountain spotted fever, plague and cholera. Insecticide use for disease control has also opened up vast land areas for human habitation.

#### Knowledge of Adverse Effects Lacking

Much is alleged but little is known about chronic adverse health effects resulting from acute toxicity, or from long term exposure to small amounts of pesticides. One promptly meets voids and inadequacies of factual information in this area. A few pesticides are known to cause tumors or to be carcinogenic for fish, mice, rats or dogs, under experimental conditions. There are no known carcinogenic pesticides for man other than the arsenics. In birdlife, rats and dogs, the chlorinated hydrocarbons have been shown to have adverse reproductive effects in terms of frequencies and survival of newborn. Pesticides have been called mutagens responsible for adverse hereditary effects, and have been said to be contributing to congenital diseases. Substantiating data on this is not known. They have also been accused of causing a number of other chronic disease processes. In one of these conditions, blood dyscrasias, lindane has been shown to be directly or circumstantially implicated. There are a number of DDT toxicity studies involving volunteers and formulating industrial workers who received intakes of 35 mg. per day (about 200 times the normal) for some months and had levels of DDT and metabolites in their fat averaging 270 ppm, without evidence or ill effects during a follow-up period of 18 months.

Methoxychlor has also been given to humans over an eight-week period at a daily rate of 0.5–2.0 mg/kg of bodyweight without evidence of toxicity. However, it is prudent to recognize that in man there usually is a period of years between the initiation and the manifestation of chronic diseases including cancer. Subtle genetic aberrations, carcinogenic effects, reproductive and congenital defects and

chronic disease symptomatology possibly resulting from pesticides could readily remain undetected. Also in these kinds of disease processes the "norms" are in constant change from numerous factors such as alterations in the population make-up, in social behaviorial and medical practices, and in other etiologic agents that produce the same diseases. To date most of the alleged adverse health effects in humans, other than acute toxic effects, resulting from pesticides are by implication and assumption and not by established fact. However, a position that pesticides do not possess significant chronic health hazards also rests on an uncertain base.

#### Recent Accidents Noteworthy

Some current noteworthy accidents are; in Sept 1967 there were 17 parathion deaths and many more acute illnesses at Tijuana, Mexico. In a government warehouse, liquid parathion containers leaked and contaminated flour and sugar later used in a Tijuana bakery. In Nov, liquid parathion being trucked in cartons contaminated several bags of baking powder used to make bread at Chquinquirá near Bogota, Columbia. The initial estimates were that about 1,000 persons consumed some of the bread, 600 became ill, and 300 were in serious condition. At the time of the report, there were 80 deaths. In Nov, 7 deaths occurred in children of one family in Florida from parathion. The father has been indicted for homicide so these 7 deaths probably are not accidental. The 2 accidental events suggest a series of weak areas in safety controls, including the need for color indicators in liquid compounds. In recent years in California, diazinon contaminated bakery flour and caused 17 acute poisonings with no deaths; and phosdrin, while being trucked, contaminated children's wearing apparel which poisoned 2 sales clerks and 5 children who handled the clothes.

#### Comment and Summary

The scientific application of pesticides to world food and disease problems has made and will continue to make major contributions to the world's health and well-being.

Pesticides are toxic agents to all forms of life, including human, and their use, or more properly their misuse, is causing a sizeable annual body of morbidity and mortality. In the United States this is amounting to about 30,000 accidental poisonings, in excess of 110 accidental deaths, and an equal or greater number of nonaccidental deaths. The acute toxic health problem is quite well understood. It is



basically remedial through strict adherence to recommended safety measures and practices, and through more effective public information programs that will result in constant isolation of pesticides from children.

Unwanted residuals of pesticides are occurring in man's food and elsewhere in his daily environment on a world-wide basis. While it appears that pesticides do not have a significant health hazards resulting from long term minute exposures, this viewpoint is not based on any reasonably adequate body of scientific pesticide health knowledge. It is a judgment

and is subject to the errors of judgment exercised in areas of unknown. There is particular need for intensive research on the short and long term effects of pesticides on man's vital tissues and systems, and for short and long term epidemiological studies on populations at high and low risks to confirm or deny what, if any, diseases are resulting from or being adversely affected by pesticides. In the interest of the future health of the public and of the industry, more influence should be brought to bear on the development of additional research programs in pesticides and human health.

## KNOW YOUR WORLD

### Did You Know?

That the area of the United States in which a person lives plays some part in determining how long he lives?

The National Center for Chronic Disease Control indicates that the death rates of middle-aged Americans differ strikingly among geographical sections of the country. For white American men, 45-64 years old, the risk of dying in certain areas is about double that in others, and is particularly true for rates pertaining to all causes of death as well as to cardiovascular disease. The highest-death-rate areas are along the East Coast, while the lowest rates are found west of the Mississippi, particularly the Great Plains. Studies of 1949-1951 and 1959-61 show that sections of East Central Pennsylvania are consistently among the country's highest-death-rate areas. Very low rates are in parts of Nebraska and sections running from Minnesota to Texas. The Heart Disease and Stroke Control Program is investigating reasons for these geographic differences in the risk of dying from heart disease. Factors include diet, smoking habits, blood pressure, high levels of cholesterol in the blood, overweight, physical activity, physical environment and "stress and strain" of cultural conflict.<sup>1</sup>

That although poliomyelitis has been dramatically reduced in Europe, North America and Oceania, it is still on the increase in most other parts of the world?

In 44 tropical and semi-tropical countries, 9,043 cases occurred in 1966, compared to an average of 3,006 cases annually from 1951-1955.<sup>2</sup>

That the number of filariasis cases, all kinds, is estimated to be more than 200 million worldwide and is increasing daily?

The WHO Filariasis Research Unit in Rangoon is investigating the ecology, biology, and insecticide susceptibility of *Culex pipiens fatigans*, the principal vector of *Bancroftian filariasis*, with the aim of developing an economical method of reducing the vector population sufficiently to interrupt transmission of the infection.<sup>3</sup>

That 41 water supplies, serving 144,000 people in 10 States in USA, were found to have 3 or more pCi (picocuries) of radium-226 per liter?

Four supplies, serving 3,000 people, contained 10 or more pCi per liter. The highest concentration observed was 24.1 pCi per liter in a supply serving 360 people.<sup>4</sup>

That on 1 January 1968, a requirement for safety markings on transparent glass doors and fixed, adjacent transparent glass sidelights was effected in New York State?

Industrial Code Rule No. 47 requires compliance by all mercantile, commercial, factory, school, college and university buildings in the State. All State and municipal buildings come under this rule.<sup>5</sup>

That from 1 April 1967 to 1 April 1968, the U.S. Food and Drug Administration analyzed 5,263 food samples for the presence of salmonellae?<sup>6</sup>

That a yellow fever suspected outbreak in the Municipality of Abeatuba and Barcarena, southwest of Belém in Pará State of Brazil has been reported in July 1968?

The affected area lies along the Arienga River which marks the boundary between the two municipalities. Yellow fever has been isolated by the virus laboratory of Evandro Chagas Institute, from blood

specimens of 2 field laborers and 1 marmoset (*Sanguinus ursulus*). Investigation is continuing.<sup>7</sup>

#### References

1. Mass Dept Public Health Bull, "This Week in Public Health" 17(25):258, Jun 24, 1968.
2. WHO Chron 22(6):218, June 1968.
3. WHO Chron 22(6):218, June 1968.
4. Public Health Rep 33(7):551-557, July 1968.
5. Public Health Rep 33(7):622, July 1968.
6. USDHEW NCDC "Salmonella Surveillance" Rep No. 73, 13-14, June 6, 1968.
7. WHO Wkly Epid Rec 43(31):387, Aug 2, 1968.

## EDITOR'S SECTION

### HODGKIN'S DISEASE

*Med Lett Drugs Ther* 10(3): 10-12, Feb 9, 1968.

A more optimistic attitude toward the curability of Hodgkin's disease, the most common form of lymphoma, has developed in recent years, owing in large part to the effective use of megavoltage radiotherapy. The prognosis in Hodgkin's disease is related to the extent of the disease at the time of diagnosis. Determination of extent requires a review of systemic symptoms, a search for lymph node and organ involvement, roentgenographic survey of lungs and bones, and lymphangiography of pelvic and retroperitoneal lymph nodes. In Stage I the disease is limited to one anatomic region; in Stage II, to two anatomic regions on the same side of the diaphragm; in Stage III, to disease on both sides of the diaphragm, but not extending beyond lymph nodes and spleen. In Stage IV, extralymphatic tissues, such as bone marrow, lung parenchyma, liver, bone, and skin are involved, in addition to lymph nodes. Stages are further classified as "A," without symptoms, and "B," with systemic symptoms, such as fever, night sweats, pruritus, and weight loss (S. A. Rosenberg, *Cancer Res.*, 26:1310, 1966).

**Radiation Therapy**—Localized x-ray therapy is the primary treatment of Hodgkin's disease. The results depend on the stage in which treatment is initiated. Stages I and IIA have a far better prognosis than Stages IIB, III and IV. With the use of more radical radiotherapy, survival time has improved steadily (H. S. Kaplan, *Cancer Res.*, 26:1221, 1966). For Stage I patients, E. C. Easson and M. H. Russell (*Brit. Med. J.*, 1:1704, 1963) report 40 percent survival beyond 10 to 15 years with doses of radiation above 2500 rads; patients surviving beyond 10 years without recurrences may be regarded as cured.

The present trend is to give high doses of x-rays (3000 to 4000 rads in three to four weeks) to the

known areas of disease and to adjacent areas. In most instances Hodgkin's disease advances by direct extension to adjacent areas (M. V. Peters, *Cancer Res.*, 26:1232, 1966). Many patients are initially seen with systemic symptoms and widespread disease. Even in advanced cases not susceptible to cure by radiotherapy, it remains the primary treatment for local areas of disease, to alleviate discomfort, and to prevent life-threatening complications.

**Surgery**—Surgery as primary therapy of Hodgkin's disease is restricted to the rare patient in whom the disease is localized to the stomach or small intestine, especially when complicated by hemorrhage or obstruction. Supplemental radiation therapy is also advisable.

**Chemotherapy**—Chemotherapy, alone or in association with localized x-ray therapy, is indicated in the symptomatic and disseminated stages of Hodgkin's disease. With such therapy complete or partial suppression of the disease is achieved in 60 to 80 percent of patients. Effectiveness depends on the activity and the stage of the disease, and on the history of previous therapy. The response to a single course of chemotherapy usually lasts about 6 to 10 weeks, but if there is a satisfactory initial response, it may be prolonged by maintenance therapy.

The useful chemotherapeutic agents fall into four unrelated classes; when resistance to one agent develops, it usually extends to the other members of the same class. The patient may, however, respond to a drug of another type.

Mechlorethamine Hydrochloride USP (nitrogen mustard) should be given when the patient's condition demands a rapid response, as in high fever, or compression of the spinal cord or major blood vessels. Chlorambucil USP is preferred for main-



tenance therapy. Customarily the alkylating agents are used first, and when resistance develops, vinblastine is substituted. Vinblastine can, however, be used as the initial drug. In some patients refractory to these agents, procarbazine, an experimental drug, is being tried. Patients receiving chemotherapeutic agents must be followed carefully with weekly ex-

aminations and blood counts. Prednisone USP should be reserved for patients with acquired hemolytic anemia and with far-advanced, resistant disease.

The following table lists the drugs used, together with dosage recommendations, indications and toxicity.

#### PRINCIPAL CHEMOTHERAPEUTIC AGENTS USED IN HODGKIN'S DISEASE

Drug	Usual Dose <sup>1</sup>	Indications	Toxicity
Alkylating agents Mechlorethamine (nitrogen mustard) (Mustargen—Merck)	0.4 mg/kg i. v. in 1 to 4 days	Indicated for rapid relief of acute symptoms	Local necrosis if extravasated; vomiting; bone marrow depression
Triethylenethiophosphoramide (Thio-TEPA—Lederle)	0.2 to 0.4 mg/kg i. v. daily to total of 0.8 to 1 mg/kg; weekly i. v. 0.2 to 0.4 mg/kg for maintenance	Can be used instead of nitrogen mustard; it is less likely to cause vomiting	Bone marrow depression
Chlorambucil (Leukeran—Burroughs (Wellcome))	0.1 mg/kg per day orally	Maintenance therapy; dose based on response and blood picture	Bone marrow depression
Cyclophosphamide (Cytosan—Mead Johnson)	10 mg/kg i. v. daily for 4 days or 3 to 4 mg/kg daily orally	Used in patients with impaired marrow function; as i. v. or oral maintenance therapy	May produce less bone marrow depression than chlorambucil; alopecia; hemorrhagic cystitis
Vinca alkaloids Vinblastine (Velban—Lilly)	0.1 mg/kg i. v. weekly	As initial or maintenance therapy	Leukopenia; thrombocytopenia; alopecia; local necrosis if extravasated
Vincristine (Oncovin—Lilly)	0.01 to 0.02 mg/kg i. v. weekly for 3 to 5 weeks	Used in patients with impaired marrow function	Peripheral neuropathy; muscle weakness; alopecia; mild bone marrow depression
Methylhydrazine derivatives Procarbazine (Natulan—Roche) (available in the U.S. for experimental use only)	50 mg/day orally increasing within 1 week to 200 to 300 mg/day for 2 to 3 weeks; maintenance level 50 to 100 mg/day	New agent, used when alkylating agents and vinca alkaloids are no longer effective	Nausea and vomiting; bone marrow depression; mental depression
Adrenal corticosteroids Prednisone (many manufacturers)	40 to 100 mg/day orally	Used in patients with acquired hemolytic anemia; and in far-advanced resistant disease	Hyperadrenocorticism

1. Doses must be adjusted according to response and evidence of toxic effects.

#### INSECT REPELLENTS

*Med Lett Drugs Ther* 10(14):55-56  
July 12, 1968.

Insect bites can be merely an annoyance or, in some areas, the means of transmission of serious infections. When the use of insecticides and other insect control measures is impractical or unsuccessful, the application of repellents to skin and clothing can be helpful.

**Available Preparations**—The United States Department of Agriculture has tested over 9,000 chemicals for use as insect repellents and found that N, N-diethyl-m-toluamide (commonly known as deet) is the best all-purpose repellent yet developed (C.N.

Smith et al., U.S. Department of Agriculture, Pub. ARS-33-26, 1960). Other effective repellents include ethyl hexanediol, dimethyl phthalate, dimethyl carbate, and butopyronoxyl (Indalone). Most of the commercially available repellent preparations contain either deet (Off; McKesson Mosquitone; and others) or ethyl hexanediol (6-12 Brand; Skeeto-Go; and others), and they are marketed in a variety of forms, including liquid, foam, pressurized spray, stick, cream, and wipe-on tissues. Concentrations of the active ingredients vary with both type of formulation and brand; for example, preparations in which deet is the only repellent compound contain from less than 5 percent (in wipe-on tissues) to more than 40 percent (in liquids).



**Factors Affecting Repellent Action**—The concentration of the active compound in the repellent can affect both the range of susceptible insects and the duration of effect. The United States military services use 75 percent deet in both liquids and pressurized sprays. The lower concentrations of deet in commercial preparations make them less greasy and therefore more acceptable cosmetically, but more frequent applications of the repellent may be necessary.

People vary in their attractiveness to insects; men are generally more attractive to mosquitos than are women, and moist skin is more apt to be bitten than dry skin. Sweating, swimming, and wiping tend to remove repellent from the skin and increase the need for frequent application.

**Methods of Use**—The most common method of using a repellent, whether liquid, foam, or spray, is to apply it to the hands and then smear it evenly over all exposed skin. A repellent should never be sprayed directly on the face. Under favorable conditions one application will last several hours; it should be repeated when the insects are no longer repelled. It is sometimes necessary to apply the same repellent to the clothing particularly around openings; some of the repellents, however, are damaging to some synthetic fibers and plastics.

**Oral Repellents**—H. L. Mueller (in M. Samter et al., *Immunological Diseases*, Boston: Little, Brown and Company, 1965 p. 682) found that over 70 percent of 100 insect-sensitive patients reported that insects bothered them little or not at all when they were taking a daily dose of 75 to 150 mg thiamine hydrochloride. Controlled studies are necessary, however, before thiamine can be recommended as an oral repellent.

**Adverse Effects**—Since no medical claims are made for insect repellents, they are not subject to regulations of the Food and Drug Administration as to either safety or effectiveness. Considering the extensive use of repellents, there have been very few reports of toxic and hypersensitivity reactions caused by the active agents or other components of repellent preparations. Insect repellents are absorbed through intact skin, but it is unlikely that

under ordinary circumstances such absorption is sufficient to produce systemic toxicity. In a case report by J. Gryboski et al. (*New Eng. J. Med.*, 264:289, 1961) a toxic encephalopathy was noted in a three-year old child after exposure to a total of six ounces of a repellent containing 15 percent deet which had been sprayed on the child and her bed clothes for a period of two weeks. Particular caution should be taken about applying repellent preparations to children and infants since they are prone to lick any material applied to the skin; bottles should be kept out of reach to avoid ingestion of liquid preparations. Any of the repellents may cause smarting when applied to mucous membranes. If they get into the eyes, they can produce severe stinging; whether permanent ocular injury can be produced is unknown. Contact dermatitis occurs occasionally.

#### BUMED FILM RELEASES

The following new films may be found in Hospital Film Libraries and Training Aids Centers:

MN-10494 — *Trip to Where* — 16mm — color, sound, 49 minutes. Film presents dangers of use and abuse of three basic groups of drugs; namely, amphetamines, barbiturates and hallucinogens, including marijuana and emphasizing lyseric acid diethylamide or LSD. Points out psychological and physical effects, especially in relation to potentially dangerous effects on individual performance in critical operations.

MN-9778 E—*Mental Meath and Military Effectiveness: Journey to the Bottom*—16mm, B & W, sound, 50 minutes. Documents three case studies of depression reaction and demonstrates the effects of this reaction on function in the naval environment. Depicts management and disposition of each case, emphasizing dynamics of depression reaction.

MN-10284—*Careers in Medicine: The Submarine and Diving Medical Officer*—16mm-color, sound, 38 minutes. Describes the training, the variety of work performed, and the professional growth potentials available to the Submarine and Diving Medical Officer.

**DEPARTMENT OF THE NAVY**

POSTAGE AND FEES PAID  
DEPARTMENT OF THE NAVY

BUREAU OF MEDICINE AND SURGERY  
WASHINGTON, D.C. 20390

OFFICIAL BUSINESS

PERMIT NO. 1048